Original Article

Does Talc Reduce Seroma Formation after Mastectomy: A Randomized Controlled Trial

Ronnarat Suvikapakornkul MD, MSc[1], Rungkij Chaiteerakij MD[1],
Panuwat Lertsithichai MD, MSc[1], Yodying Wasutit MD[1]

[1] Breast and Endocrine Surgery Unit, Department of Surgery, Faculty of Medicine, Ramathibodi Hospital, Mahidol University

Background: The most common complication following mastectomy is seroma formation. Surgeons tend to leave the drain longer to prevent seroma but it will increase rate of infection and patient's discomfort.

Objective: The aim of the present study was to evaluate the efficacy of talc in reducing drain volume and shorten duration of drain in comparison to the routine care.

Materials and Methods: Patients with breast cancer undergoing mastectomy were randomly assigned to TALC and NON-TALC group. For the TALC group, talc was applied in the mastectomy space, and none was given in the NON-TALC group. The total volume of drain, day of leaving drain, seroma formation, complications and long-term recurrence were recorded.

Results: Fifty-two patients were randomly assigned in two groups equally. Talc did not show any correlation to the reduction of drain fluid (910 mL for NON-TALC group vs. 912.5 mL for TALC group; $p = 0.583$). TALC and NON-TALC group demonstrated no difference in duration of drainage (16.5 days vs. 15.5 days; $p = 0.437$). However, one seroma was found in NON-TALC. Overall, there was no different loco-regional and distant recurrence in both groups.

Conclusion: There was no sufficient evidence to support the application of talc following mastectomy to reduce the drainage volume and decrease the duration of draining.

Keywords: Mastectomy, Seroma, Drain, TALC

J Med Assoc Thai 2018; 101 (7): 965-70
Website: http://www.jmatonline.com

Breast cancer is a common neoplasm for women worldwide. Mastectomy and axillary staging plays an important role in surgical treatment of early breast cancer, even in the breast-conserving era. The potential complications following mastectomy with or without axillary dissection are lymphorrhea, seroma, hematoma, and wound infection[1].

Seroma is an abnormal collection of serous fluid, associated to patient discomfort, delayed wound healing, skin necrosis, and infection[2]. The incident rate of seroma varies from 15 to 90 percent[3]. The surgeons tend to leave the drain in longer to prevent seroma formation, but this will increase the rate of infection and give patients discomfort.

Numerous methods have been used to reduce the incidence of seroma formation. The instruments used for performing surgery have effects on the seroma formation. Electrosurgical unit for hemostasis is a preferable method due to shorten operative time and less blood loss, but it is associated with more seroma formation in comparison to knife dissection[4,5]. Other techniques includes argon diathermy, laser scalpel and ultrasonic coagulation which did not show results any better than knife dissection[6-8]. Electrothermal bipolar vessel sealing system showed excellent results in seroma prevention[9]. The external compression dressing has no benefit for reducing seroma[10,11]. Various methods of suturing have been used for closing the dead space. Several randomized controlled trials demonstrated promising results; there were reduction in seroma formation and drainage duration[12-15].

Chemicals has been used for reducing seroma. Many of the trials were meta-analysis report with results showing that fibrin glue does not reduce seroma[16-18]. However, a few studies revealed some benefits[19,20]. Tetracycline also had no effect in reducing seroma[21]. The use of sclerosing agent is not

Correspondence to:

Suvikapakornkul R. Breast and Endocrine Surgery Unit, Department of Surgery, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Rajthewi, Bangkok 10400, Thailand.
Telephone: +66-2-2011527, **Fax:** +66-2-2011527 ext. 214
Email: tersv@mahidol.ac.th

How to cite this article: Suvikapakornkul R, Chaiteerakij R, Lertsithichai P, Wasutit Y. Does talc reduce seroma formation after mastectomy: a randomized controlled trial. J Med Assoc Thai 2018;101:965-70.

popularized because there is no clear benefit.

OK-432 (Sapylin) is widely accepted for its benefit in reducing ascites fluid and plural effusion in patients with metastatic carcinoma[22]. It can reduce drainage volume and the duration as well as decrease the incidence of seroma after removal of the drain[23]. Methylprednisolone administered into the surgical space was effective in reducing seroma in mastectomy and sentinel lymph node biopsy patients but the effect was not demonstrated in mastectomy and axillary lymph node dissection group[24].

Talc is the safest and cost effective sclerosant for pluerodesis[25]. The role of talc for reducing seroma formation has been used in hernia surgery but the results were inconsistent[26,27]. Talc can be used safely in modified radical mastectomy but there was no sufficient evidence to support its use for seroma prevention and reduce drainage duration[28].

The present study had been designed to evaluate the efficacy and safety of talc for reducing drainage fluid in comparison to no applying talc. Secondary end points were to evaluate the efficacy of talc to reduce seroma formation and the loco-regional and distant metastasis in long term.

Materials and Methods

Between April 2013 and October 2013, the randomized double-blinded controlled trial was conducted at the Breast and Endocrine unit, Department of Surgery, Faculty of Medicine, Ramathibodi Hospital, Mahidol University. The study protocal was approved by The Research and Ethics Board of Faculty of Medicine, Ramathibodi Hospital.

The present study enrolled 52 women who were pathologically confirmed as having breast carcinoma. All of these patients were considered to receive mastectomy and sentinel lymph node biopsy with or without axillary lymph node dissection depending on the results of intraoperative frozen section of nodes. Exclusion criteria included pregnancy, history for allergy to talc and those who had undergone preoperative radiation. All of the participants gave their informed consents. Cancer staging was classified by using the American Joint Committee on Cancer [AJCC] system, 7th edition.

The randomized number was generated by a computer and concealed in the envelopes. The patients underwent mastectomy by dissection of cutaneous flaps, removing glandular tissue including pectoralis fascia with an electrocautery dissection. The sentinel lymph node biopsy was performed with a combined injection of 2 mL of the radioisotope and 2 mL of 1% isosulphan blue at the subareolar site. If the macro-metastasis was found by the intraoperative frozen section, level I and II axillary node dissection would be performed. Before skin closure, the envelope was opened and the randomly generated number was obtained. The patients were divided into two groups: TALC and NON-TALC.

In TALC group, 4-gram of sterile dry talc was put in the Asepto bulb irrigation syringe and applied into the entire raw surface of the mastectomy site. The talc was not washed out. In NON-TALC group, nothing was given. At the end of the procedure, two closed, low-pressure suction drains were placed under the skin flap and in the axillary space.

All the patients were monitored post-operatively for pain, bleeding and infection in the hospital for 48 to 72 hours. They were instructed to record daily output, wound care, early shoulder exercise and drain care to assure patency as home care basis. Each patient returned to the out-patient unit to monitor for complications weekly and have their daily fluid drainage reviewed. Both the patient and the doctor who followed up were under blinded circumstances. Drains were removed when the output was less than 30 mL per day in 3 consecutive days. In the case of clinical detection of seroma after having the drainage removed, tapping procedure for release was performed. The patients were follow-up every 3 to 6 months to detect local and distance recurrence.

Statistical Analysis

The authors planned to recruit 50 participants that would have a 90% chance of detecting and 30% reduction in drainage volume using a two-tailed test at the 5% level of significance. For descriptive statistics, mean or median with standard deviation was applied. Categorical variables were described in percentage. Bivariate analysis was conducted using Student's t test, Fisher exact test, and the Chi-square test. For the continuous outcome, the authors used Wilcoxon rank sum test. A p-value ≤ 0.05 was considered statistically significant. Statistical analysis was using STATA statistical software.

Results

The 52 women with breast carcinoma were randomly allocated in two groups equally. There were no differences in the patients' characteristics of the two groups, except that there was higher staging in TALC group (Table 1). The Table 2 demonstrated the total

drain volume and the duration of drain which revealed no difference in both groups. The aspiration was done only one time in the patient with seroma and there was no recurrence after having gone through the sequential follow-up. There were no other complications in all patients. The median follow-up time was 54 (2 to 66) months. There was no locoregional recurrence in both groups and distance recurrences were not statistically significant.

Discussion

The data suggest that application of talc into the mastectomy space with or without axillary lymph node dissection does not reduce the drainage fluid and does not shorten the duration of drain placement.

It is known to the surgeon that seroma is a common complication in mastectomy even with or without axillary lymph node dissection. Seroma is not lethal, but gives both the surgeon and patient discomfort. Aspiration is usually performed in all palpable or ballottable fluid collection. The frequency of aspirations ranged from 0 to 5 times[29]. The aspirate volume per patient ranged from 95 to 300 ml[30].

The use of drain effectively decreases seroma formation but increases the cost of medical care, nursing time, rate of infection, duration of hospital stay, and essentially, the quality of life[31]. After putting multiple factors into consideration, surgeons and patients should carefully choose a suitable strategy to deal with seroma. In the authors' institution, drains are routinely placed, early discharge is given for drainage in situ and removed if the amount of fluid was less than 30 ml per day in 3 consecutive days. Any effective strategy to reduce drain fluid, shorten the time until drain removal and prevent seroma could improve quality of care.

Talc or hydrous magnesium silicate ($Mg_3Si_4O_{10}(OH)_2$) is a chemical compound with varying amounts of calcium, aluminum and iron[32]. Talc particles demonstrate a wide range of sizes from 10.8 µm to 33.6 µm. Talc is effectively and safely used for pleurodesis in malignant pleural effusion for a long time[25]. There are no long term complications or malignant formation for 22 to 35 years after pleural talc application[33]. Pleural cavity has higher absorptive capacity than subcutaneous tissue, hence, it can be assumed that talc applied to the subcutaneous tissue will be safe and give no systemic effects.

The effectiveness of using talc for reducing drain volume and seroma in the subcutaneous tissue surgery is still a controversy. There were case reports demonstrated the effectiveness of talc for the treatment of chronic seroma of the subcutaneous tissue[34,35]. According to ventral hernia surgery with wide subcutaneous tissue dissection, application of talc helped drains to be removed earlier (14.6 vs. 25.6 days; $p<0.001$) with dramatic reduction in postoperative seromas requiring intervention and did not increase

Table 1. Patient characteristics information

Variables	Non-TALC Group (n = 26)	TALC Group (n = 26)	*p-value*
Age (year); mean ± SD	55.96±12.79	60.15±8.55	0.171
Body mass index; mean ± SD	24.52±4.88	24.03±4.24	0.704
Stage of cancer; n (%)			
I	5 (19.23)	10 (38.46)	0.042
II	14 (53.85)	5 (19.23)	
III	7 (26.92)	9 (34.62)	
IV	0	2 (7.69)	
Mastectomy and SLNB only; n (%)	9 (34.62)	12 (46.15)	0.397
Mastectomy and ALND; n (%)	17 (65.38)	14 (53.85)	
Neoadjuvant chemotherapy; n (%)	1 (3.85)	5 (19.23)	0.083

Table 2. Factors related outcomes of interested

	Non-TALC Group (n = 26)	TALC Group (n = 26)	*p*-value
Total drainage volume (mL); median (range)	910 (245-4880)	912.5 (350-2397)	0.583
Duration leaving drain (days); median (range)	15.5 (10-31)	16.5 (8-41)	0.437
Seroma formation	1	0	0.610
Distant recurrence; n (%)	2 (7.69)	5 (19.23)	0.220

postoperative complications[26]. This is in contrast to the study done by Paramesrawan et al[27], which showed that the application of talc increased the rate of seroma formation and superficial wound infection in the 21-patients whom underwent open onlay repair of large abdominal wall hernia.

Mastectomy with or without axillary surgery are under the category of subcutaneous surgery. Currently, there are few reports of effectiveness of talc for reducing seroma in this kind of surgery. The application of talc in the axillary dissection in a porcine model decreased the drain duration, drain volume and prevented seroma formation without complications. In the laboratory and histologic study, talc particles contained in macrophages migrated to the spleen without any effect to the spleen[36]. There are some reports that demonstrate success in using talc for the treatment of chronic seroma following breast surgery[37,38]. The randomized study by Garza-Gangemi et al demonstrated the application of talc did not prevent seroma formation following modified radical mastectomy[28].

In the present study, we also recruited the patients who only underwent sentinel lymph node biopsy without axillary lymph node dissection; a situation that could happen in the real clinical practice. This was different from the study by Garza-Gangemi et al[28] which only has patients with axillary lymph node dissection. The total drain volume of the sentinel lymph node only is less than that of axillary dissection group. The efficacy of talc might increase in these patients. Nevertheless, the present study did not demonstrate that application of talc in the mastectomy space was able to reduce drainage volume or reduce drainage duration. From the authors current knowledge, this is the first study that shows the talc application does not increase loco-regional recurrence and does not have any effect on distant metastasis in long term follow-up.

Conclusion

There was not sufficient evidence to support the application of talc following mastectomy to reduce the drainage volume and decrease the duration of draining. Talc application does not increase rate of cancer recurrence.

What is already known on this topic?

The knowledge that talc does not reduce the drainage volume in the mastectomy. Unlike the other application that used talc in the subcutaneous surgeries (i.e., hernia surgery) have some evidences that it can reduce fluid drainage.

What this study adds?

This is the study to evaluate the efficacy of applying talc in the mastectomy wound for reducing drainage volume, the results were no difference in volume and duration of drain from the NON-TALC group. Finally, the study adds the knowledge that talc does not increase an incident of cancer recurrence in 5 years' duration.

Acknowledgement

The present research project would not have been possible without the support of many people. The authors wish to express sincere thank to the all of the surgical residents and all of the nurses in the operating room who were abundantly helpful and offered invaluable assistance and support.

Potential conflicts of interest

The authors declare no conflict of interest.

References

1. Budd DC, Cochran RC, Sturtz DL, Fouty WJ Jr. Surgical morbidity after mastectomy operations. Am J Surg 1978;135:218-20.
2. Aitken DR, Minton JP. Complications associated with mastectomy. Surg Clin North Am 1983;63:1331-52.
3. Osteen RT, Karnell LH. The National Cancer Data Base report on breast cancer. Cancer 1994;73:1994-2000.
4. Porter KA, O'Connor S, Rimm E, Lopez M. Electrocautery as a factor in seroma formation following mastectomy. Am J Surg 1998;176:8-11.
5. Keogha GW, Doughty JC, McArdle CSM, Cooke TG. Seroma formation related to electrocautery in breast surgery: a prospective randomized trial. Breast 1998;7:19-41.
6. Kerin MJ, O'Hanlon DM, Kenny P, Kent PJ, Given HF. Argon-enhanced cutting and coagulation confers advantages over conventional electrocautery for mastectomy. Eur J Surg Oncol 1996;22:571-3.
7. Wyman A, Rogers K. Randomized trial of laser scalpel for modified radical mastectomy. Br J Surg 1993;80:871-3.
8. Deo SV, Shukla NK. Modified radical mastectomy using harmonic scalpel. J Surg Oncol 2000;74:204-7.
9. Manouras A, Markogiannakis H, Genetzakis M,

Filippakis GM, Lagoudianakis EE, Kafiri G, et al. Modified radical mastectomy with axillary dissection using the electrothermal bipolar vessel sealing system. Arch Surg 2008;143:575-80.
10. O'Hea BJ, Ho MN, Petrek JA. External compression dressing versus standard dressing after axillary lymphadenectomy. Am J Surg 1999;177:450-3.
11. Chen CY, Hoe AL, Wong CY. The effect of a pressure garment on post-surgical drainage and seroma formation in breast cancer patients. Singapore Med J 1998;39:412-5.
12. Garbay JR, Thoury A, Moinon E, Cavalcanti A, Palma MD, Karsenti G, et al. Axillary padding without drainage after axillary lymphadenectomy - a prospective study of 299 patients with early breast cancer. Breast Care (Basel) 2012;7:231-5.
13. Sakkary MA. The value of mastectomy flap fixation in reducing fluid drainage and seroma formation in breast cancer patients. World J Surg Oncol 2012;10:8.
14. Kottayasamy SR, Gupta V, Singh G. Prevention of seroma formation after axillary dissection--a comparative randomized clinical trial of three methods. Breast J 2013;19:478-84.
15. Almond LM, Khodaverdi L, Kumar B, Coveney EC. Flap anchoring following primary breast cancer surgery facilitates early hospital discharge and reduces costs. Breast Care (Basel) 2010;5:97-101.
16. Udén P, Aspegren K, Balldin G, Garne JP, Larsson SA. Fibrin adhesive in radical mastectomy. Eur J Surg 1993;159:263-5.
17. Vaxman F, Kolbe R, Stricher F, Boullenois JN, Volkmar P, Gros D, et al. Biological glue does not reduce lymphorrhoea after lymph node excision. Randomized prospective study on 40 patients. Ann Chir 1995;49:411-6.
18. Carless PA, Henry DA. Systematic review and meta-analysis of the use of fibrin sealant to prevent seroma formation after breast cancer surgery. Br J Surg 2006;93:810-9.
19. Gilly FN, Francois Y, Sayag-Beaujard AC, Glehen O, Brachet A, Vignal J. Prevention of lymphorrhea by means of fibrin glue after axillary lymphadenectomy in breast cancer: prospective randomized trial. Eur Surg Res 1998;30:439-43.
20. Jain PK, Sowdi R, Anderson AD, MacFie J. Randomized clinical trial investigating the use of drains and fibrin sealant following surgery for breast cancer. Br J Surg 2004;91:54-60.
21. Rice DC, Morris SM, Sarr MG, Farnell MB, van Heerden JA, Grant CS, et al. Intraoperative topical tetracycline sclerotherapy following mastectomy: a prospective, randomized trial. J Surg Oncol 2000;73:224-7.
22. Kitsuki H, Katano M, Ikubo A, Morisaki T, Anann K, Tanaka M, et al. Induction of inflammatory cytokines in effusion cavity by OK-432 injection therapy for patients with malignant effusion: role of interferon-gamma in enhancement of surface expression of ICAM-1 on tumor cells in vivo. Clin Immunol Immunopathol 1996;78:283-90.
23. Yang Y, Gao E, Liu X, Ye Z, Chen Y, Li Q, et al. Effectiveness of OK-432 (Sapylin) to reduce seroma formation after axillary lymphadenectomy for breast cancer. Ann Surg Oncol 2013;20:1500-4.
24. Qvamme G, Axelsson CK, Lanng C, Mortensen M, Wegeberg B, Okholm M, et al. Randomized clinical trial of prevention of seroma formation after mastectomy by local methylprednisolone injection. Br J Surg 2015;102:1195-203.
25. Shaw P, Agarwal R. Pleurodesis for malignant pleural effusions. Cochrane Database Syst Rev 2004;(1):CD002916.
26. Klima DA, Brintzenhoff RA, Tsirline VB, Belyansky I, Lincourt AE, Getz S, et al. Application of subcutaneous talc in hernia repair and wide subcutaneous dissection dramatically reduces seroma formation and postoperative wound complications. Am Surg 2011;77:888-94.
27. Parameswaran R, Hornby ST, Kingsnorth AN. Medical talc increases the incidence of seroma formation following onlay repair of major abdominal wall hernias. Hernia 2013;17:459-63.
28. Garza-Gangemi AM, Barquet-Munoz SA, Villarreal-Colin SP, Medina-Franco H, Cortes-Gonzalez R, Vilar-Compte D, et al. Randomized phase II study of Talc versus iodopovidone for the prevention of seroma formation following modified radical mastectomy. Rev Invest Clin 2015;67:357-65.
29. Soon PS, Clark J, Magarey CJ. Seroma formation after axillary lymphadenectomy with and without the use of drains. Breast 2005;14:103-7.
30. Classe JM, Berchery D, Campion L, Pioud R, Dravet F, Robard S. Randomized clinical trial comparing axillary padding with closed suction drainage for the axillary wound after lymphadenectomy for breast cancer. Br J Surg 2006;93:820-4.

31. He XD, Guo ZH, Tian JH, Yang KH, Xie XD. Whether drainage should be used after surgery for breast cancer? A systematic review of randomized controlled trials. Med Oncol 2011;28 Suppl 1:S22-30.
32. Hildick-Smith GY. The biology of talc. Br J Ind Med 1976;33:217-29.
33. Lange P, Mortensen J, Groth S. Lung function 22-35 years after treatment of idiopathic spontaneous pneumothorax with talc poudrage or simple drainage. Thorax 1988;43:559-61.
34. Holthouse DJ, Chleboun JO. Talc serodesis--report of four cases. J R Coll Surg Edinb 2001;46:244-5.
35. Lehr SC, Schuricht AL. A minimally invasive approach for treating postoperative seromas after incisional hernia repair. JSLS 2001;5:267-71.
36. Klima DA, Belyansky I, Tsirline VB, Lincourt AE, Lipford EH, Getz SB, et al. Application of subcutaneous talc after axillary dissection in a porcine model safely reduces drain duration and prevents seromas. J Am Coll Surg 2012;214:338-47.
37. Saeb-Parsy K, Athanassoglou V, Benson JR. Talc seromadesis: a novel technique for the treatment of chronic seromas following breast surgery. Breast J 2006;12:502-4.
38. Catsman CJ, Beek MA, Rijken AM. Talc seromadesis in patients with chronic seroma formation after breast surgery. Springerplus 2016;5:3.