Systematic review and meta-analysis of the use of fibrin sealant to prevent seroma formation after breast cancer surgery

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CRD summary
This review investigated the efficacy of fibrin sealants in decreasing the volume of drainage output and rate of seroma formation following breast cancer surgery. The authors concluded that the current evidence does not support the use of fibrin sealant in breast cancer surgery to achieve these outcomes. The authors’ conclusions are appropriately cautious given the limitations of the included studies.

Authors’ objectives
To investigate the efficacy of fibrin sealants in decreasing the volume of drainage output and rate of seroma formation following breast cancer surgery.

Searching
MEDLINE and EMBASE were searched for studies reported in English up to June 2005, as was the Cochrane CENTRAL Register (Issue 3, 2005); the search terms were reported. The websites of manufacturers were searched, experts were contacted, and the reference lists of relevant papers were checked.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Studies investigating fibrin sealant, delivered directly to the wound surface in liquid or aerosol form, were eligible for inclusion. Studies investigating bandages or pads impregnated with lyophilised fibrin sealant components were not included. The majority of the included studies investigated Tisseel or its market variants Tissucol and Haemaseel and, with the exception of one study, a spray device was used. The volume of sealant applied ranged from 2 to 24 mL.

Participants included in the review
Studies of women undergoing breast cancer surgery were eligible for inclusion. The most frequently performed surgery in the included studies was modified radical mastectomy (MRM); four studies exclusively investigated this population group. The remaining studies were of MRM, lumpectomy, axillary lymph node dissection, segmental mastectomy and total mastectomy. The mean or median age of the participants ranged from 50.9 to 73.0 years. The studies varied in the use of compression dressings, the number and type of drains, and the extent of shoulder mobilisation post-surgery.

Outcomes assessed in the review
Studies reporting the development of seroma and volume of drainage output as outcomes were eligible for inclusion. The secondary outcomes of interest were the number of drainage days, frequency of wound infection and length of stay in hospital.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Two authors independently assessed the studies for allocation concealment, method of randomisation, double-blinding and participant withdrawal. Any disagreements were resolved by consensus.
Data extraction
The data were extracted using a data extraction form. Relative risks (RRs) and risk differences, along with 95% confidence intervals (CIs), were calculated for dichotomous data and weighted mean differences (WMDs) for continuous outcomes. Continuous data were not included in the analysis if standard deviations or standard errors could not be calculated. The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
How were the studies combined?
The studies were pooled in meta-analyses using a random-effects model. A fixed-effect analysis was also reported where the test for statistical heterogeneity was not statistically significant. Egger's test was used to investigate the possibility of publication bias.

How were differences between studies investigated?
Subgroup analyses were planned to investigate the impact of factors such as type of surgery, and type and volume of fibrin sealant used. However, these were considered uninformative because of the small number of included studies. The Q statistic was used to investigate statistical heterogeneity (a p-value of 0.1 or less was defined as statistically significant).

Results of the review
Eleven RCTs (n=577) were included.

The methodological quality of the included trials was described as poor: allocation concealment was inadequate in all of the trials; one reported the method of randomisation; none had double-blinding; six reported complete follow-up. The trials were generally small and might have been underpowered to detect an effect.

There was no statistically significant difference between fibrin sealant and control in seroma formation (10 trials) post-surgery, though there was a trend towards an increased risk with the intervention (RR 1.14, 95% CI: 0.88, 1.46). There was no statistically significant difference between sealant and control in the volume of drainage (5 trials), though there was a trend towards a decrease with the intervention (WMD -117.7 mL, 95% CI: -259.2, 23.8). There was evidence of statistical heterogeneity in the volume of drainage analysis.

There was no statistically significant difference between fibrin sealant and control in the number of days of drainage (4 trials), wound infection (5 trials), or duration of hospital stay (4 trials). There was evidence of statistical heterogeneity in all the analyses except wound infection.

Cost information
One trial reported costs of US$440 per patient for fibrin sealant treatment, one reported costs ranging from US$190 to US$2,160, and one reported costs of US$240 per patient. In one trial comparing the costs of sealant with conventional drain placement, the incremental cost of the sealant treatment was US$366 when one drain was used and US$293 when two drains were used.

Authors' conclusions
The current evidence does not support the use of fibrin sealant in breast cancer surgery to reduce post-operative drainage or seroma formation.

CRD commentary
The review addressed a clear research question using defined inclusion criteria. Relevant sources were searched for studies, though the restriction to English language studies led to the loss of relevant data. However, there was no indication of publication bias. Appropriate measures were used to reduce error and bias in the quality assessment, but it was unclear whether similar methods were used at the study selection and data extraction stages. The methodological
quality of the included studies was assessed and their limitations discussed. Heterogeneity was investigated, although exploration of the sources of heterogeneity was limited by the small number of trials available and the several potential sources of diversity. The authors' conclusions are appropriately cautious given the limitations of the included studies.

**Implications of the review for practice and research**

Practice: The authors stated that there was no evidence to support the use of fibrin sealant in breast cancer surgery to prevent seroma formation or reduce the volume of post-operative drainage.

Research: The authors stated that large RCTs may be warranted in this field.

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