Use of tissue glue for surgical incision closure: a systematic review and meta-analysis of randomized controlled trials


CRD summary
The authors concluded that infection rates were comparable between tissue glue and standard wound closure methods. The risk of wound dehiscence and costs increased with tissue glue. The authors’ conclusions reflect the evidence, but interpretation should take into consideration the limitations of the included studies (such as heterogeneity and small samples).

Authors’ objectives
To compare the effects of tissue glue with standard wound closure methods for closure of skin incisions in the elective surgical setting.

Searching
PubMed, EMBASE and The Cochrane Library databases and Google Scholar were searched up to July 2009 for publications in English. Search terms were reported. The related-articles function in PubMed was used and references of retrieved articles were searched manually.

Study selection
Randomised controlled trials (RCTs) that compared tissue adhesives with each other types of adhesives or standard wound closure methods (such as sutures, staples and adhesive tape) after surgical skin incision in an elective setting were eligible for inclusion. Eligible trials were required to report data on one of time for wound closure, wound infection, wound dehiscence, cosmetic scoring systems and patient satisfaction. Trials of participants with traumatic lacerations were excluded.

Included trials were conducted between 1989 and 2009. Most of the included studies were of adults with reported mean ages that ranged from 24 to 72 years. Trials of children reported mean ages that ranged from three to six years. Patients underwent one of 14 different types of operation. Where reported, wound length ranged from 5mm to 250mm. Most studies used 2-octyl-cyanoacrylate as tissue glue and some used n-butyl-cyanoacrylate. The type of standard closure was skin suture (monofilament or braided suture and, where reported, using interrupted or subcuticular methods) and/or skin clips; some also received adhesive tape.

The authors did not state how many reviewers screened studies for inclusion.

Assessment of study quality
Two reviewers independently assessed study quality based on randomisation, allocation concealment, blinding, completeness of data and freedom from selective outcome reporting. The maximum score was 5. Trials that scored 3 or more were considered high quality. Discrepancies were resolved by consensus or referral to a third reviewer.

Data extraction
Two reviewers independently extracted dichotomous data (such as wound infection and wound dehiscence) to calculate risk ratios (RRs) and 95% confidence intervals (CIs). Discrepancies were resolved by consensus.

Methods of synthesis
Where meta-analysis was appropriate, either a fixed-effect model (no evidence of substantial heterogeneity) or a random-effects model (evidence of substantial heterogeneity) was used to pool relative risks and 95% CIs. Statistical heterogeneity was assessed using the $I^2$ statistic.

Subgroup analyses were undertaken according to trial quality, type of standard wound closure, type of tissue glue and type of operative procedure. Sensitivity analyses were performed by removal of outlying trials identified from funnel
Where meta-analysis was not appropriate, findings were reported as a narrative synthesis.

Results of the review
Twenty-six RCTs were included in the review and included 2,105 patients (range 14 to 209) and 2,637 wounds. Nineteen trials (18 according to the table) were of high quality and seven (eight according to the table) were of low quality.

Time for wound closure (19 RCTs): Sixteen RCTs compared tissue glue with skin sutures and fourteen showed faster skin closure using tissue glue. Three of four RCTs that compared tissue glue with skin clips showed faster closure using skin clips. One RCT compared tissue glue with adhesive tape and showed no statistically significant difference in skin closure.

Wound infection (23 RCTs): Rates of wound infection were low. No statistically significant differences were found between tissue glue and standard wound closure (10 estimable RCTs). There was no evidence of statistical heterogeneity ($I^2=0\%$).

Subgroup analyses according to trial quality, standard wound closure type, type of tissue glue used and type of operation (where this was calculable) did not significantly alter the findings.

Wound dehiscence (20 RCTs): Dehiscence rates were low, but meta-analysis showed a statistically significantly increased rate of dehiscence in patients who received tissue glue (RR 3.29, 95% CI 1.77 to 6.15, $I^2=14\%$; 10 estimable RCTs). Funnel plot analysis showed one outlying trial; removal of this trial did not significantly alter the results.

Subgroup analyses that compared tissue glue with interrupted sutures resulted in no significant differences. Type of glue (2-octyl-cyanoacrylate) affected the results and when one outlying trial was removed the difference became significant.

Eight of 12 RCTs that assessed patient satisfaction reported greater satisfaction with tissue glue. Cosmetic outcomes were reported in the review.

Cost information
Nine RCTs assessed cost of closure methods; seven RCTs showed that the material cost of skin closure was more expensive when tissue glue was used compared to standard wound closure methods; and two RCTs assessed costs in terms of extra theatre time and found that tissue glue was the less expensive option.

Authors’ conclusions
Infection rates were comparable between tissue glue and standard wound closure methods. There was an increased risk of wound dehiscence with tissue glue.

CRD commentary
The review question and supporting inclusion criteria were stated clearly. The literature search was limited to published articles in English, which increased risks of publication and language biases. Trial quality was assessed using appropriate criteria. Most trials were of high quality. Quality assessment and data extraction were performed in duplicate; it was unclear whether the same was true for study selection. Appropriate methods were used to combine trials and assess statistical heterogeneity. The authors acknowledged heterogeneity among trials, generally small sample sizes and the limited incidence of wound infection and dehiscence.

The authors’ conclusions seem to reflect the evidence available, but interpretation should take the limitations of the included studies into consideration.

Implications of the review for practice and research
Practice: The authors stated that tissue glue alone should not be used for closure of surgical skin incisions in place of
standard wound closure methods.

**Research**: The authors stated that further well-designed trials with adequate power were needed to investigate use of tissue glue in surgery, particularly to compare tissue glue alone versus sutures alone versus subcuticular sutures with a tissue glue dressing.

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