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The use of tissue sealant in parotidectomy: a systematic review and meta-analysis

D M Rojoa[1,2], F J Raheman[2], R Wright[1] and S Ghosh[1]

[1]Royal Oldham Hospital, Northern Alliance Care, Manchester and [2]Leicester Royal Infirmary, University Hospitals of Leicester, Leicester, UK

Abstract

Objective. Drains are used post-parotidectomy to reduce seroma and haematoma formation. Tissue-derived thrombin sealant can enable a drainless procedure, allowing for an earlier discharge, less discomfort and a more cost-efficient method. This study aimed to assess whether tissue sealant improves wound-related outcomes in parotidectomy.

Method. A systematic literature review was performed using a standardised published methodology and custom database search strategy. A fixed-effect meta-analysis of the combined complications was conducted.

Results. Thirteen studies were identified relating to parotidectomy procedures using tissue sealants, of which nine were included in the quantitative synthesis. Our analysis suggested a reduction in the complication rates, including haematoma and seroma, with drainless parotidectomy procedures involving tissue sealant use when compared with conventional procedures with post-operative drain use.

Conclusion. Fibrin sealant in parotidectomy may be used to facilitate a drainless approach, expediting recovery and offering better comfort to patients.

Main Article

Djamila Rojoa takes responsibility for the integrity of the content of the paper

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Corresponding author:
Djamila Rojoa;
Email: Djamila.rojoa@doctors.org.uk

Introduction

Parotidectomy is one of the head and neck soft-tissue surgical procedures where biological glue is increasingly being used to achieve haemostasis and prevent fluid collection.[1] Convention dictates insertion of a percutaneous drain post-surgery to close 'dead space' and allow blood and fluid to drain,[2] but this requires an overnight stay and has been associated with complications such as pain, infection, fistula formation, drain obstruction, discomfort and psychological impact.[3,4] Moreover, with regard to thyroid surgery, there is no firm evidence that drains improve patient outcome.[5] Most patients are reluctant to be discharged with a drain, and so stay in until the drain is removed.

Fibrin sealants encourage haemostasis by initiating the final stage of the anticoagulation pathway and mechanically bringing tissue surfaces together.[6] The apposition of the skin flap closes dead space, thereby preventing seroma and haematoma formation.

Therefore, fibrin sealant obviates the need for percutaneous drains, potentially allowing for out-patient parotidectomy procedures or a shorter hospital stay.[1] So far, articles published in the literature pertaining to fibrin sealant use in parotidectomy procedures are only of small sample sizes ($n < 120$), and there have been no systematic reviews specific to parotidectomy that have evaluated the use of fibrin sealants, thus precluding any formal conclusion about its efficacy and safety.

Our aim was to assess the benefits and post-operative outcomes of fibrin sealant in parotidectomy surgery, both on its own and when used in conjunction with post-parotidectomy drains as compared with conventional procedures using post-operative percutaneous drains without fibrin sealants. We also intended to evaluate the safety and efficacy of drainless parotidectomy procedures with the use of tissue sealants.

Materials and methods

Design

We pre-specified the review objectives, inclusion criteria and methods of analysis in a study protocol. We reported the review according to the Preferred Reporting Items for Systematic Review and Meta-analysis ('PRIMSA') guidelines for diagnostic test accuracy studies.[7]

Criteria for considering studies for this review

Types of studies

We included retrospective, observational, cohort or cross-sectional, and prospective studies as well as conference abstracts that assessed the use of fibrin sealants in parotidectomy with or without drains. Case reports, commentaries and letters to the editor were excluded.

Participants

We considered patients of any age and gender who had undergone parotidectomy with or without drains. We considered any type of tissue sealants used for closure of parotidectomy flaps and included the use of pressure bandages in some studies.

Conventional procedure

Percutaneous drains are traditionally placed after parotid surgery. In many centres this occurs when drain output is less than 30 ml/day or on post-operative day 3.[8] Jiang *et al.*[9] suggested that the optimum timing is when the output is less than 20 ml in 24 hours. This aims to reduce post-operative haematoma and seroma formation.[9]

Intervention

The use of fibrin sealant in parotidectomy enables the avoidance of post-operative drains. Sealants also aid the formation of blood clots due to the thrombin and fibrinogen components, reducing haematoma and seroma formation and risk of infection.[1] They expedite discharge from hospital, thus increasing the cost-effectiveness of the procedure. The studies included in our analysis have assessed the efficacy of two types of fibrin sealants: Tisseel™ and Artiss™. We have included studies that reported outcomes for fibrin sealant use alone as well as fibrin sealant paired with post-operative drain use.

Outcome parameters

In our included studies, the primary dichotomous outcome was any combination of reported complications following parotidectomy (i.e. the occurrence of major haematoma or seroma requiring surgical exploration, sialocele, post-operative infection, sepsis, flap necrosis, facial nerve weakness or facial fistula). The secondary continuous outcomes were the length of hospital stay and drain output.

Search methods for identification of studies

A literature search of electronic information sources (Medline, Embase, Cinahl) using the online search engine National Institute for Health and Care Excellence Healthcare Database Advanced Searches (hdas.nice.org.uk) was performed by two independent authors (DMR and FJR). The search was performed in June 2020 over a three-week period and without applying any language restriction. The terms included were: drainless parotidectomy, parotidectomy and parotid surgery, combined with tissue sealant, Tisseel, Artiss and drainless, as shown in Appendix 1. Requests were put into local resources for full texts.

Data collection and analysis

Selection of studies

Eligibility assessment of identified studies was performed by two review authors (DMR and FJR) independently. We screened the titles and abstracts of the studies identified during electronic searches. Relevant studies meeting the inclusion criteria for the review were selected and the full-text articles were retrieved.

Data extraction

Data extraction was undertaken by both review authors (DMR and FJR). The following data were extracted from the full texts of the selected articles: study authors, year of publication, type of study (retrospective, observational, cohort or cross-sectional, and prospective studies as well as conference abstracts), number of participants, type of surgery, the use of drains, type of sealant used, control, outcomes in terms of hospital in-stay and complications, and information about the quality assessment using the risk of bias 1 tool.

Statistical analysis and data synthesis

A table of 'events', the number of complications encountered in parotidectomy procedures with fibrin sealants versus those without, was constructed. We generated forest plots to show the variation of the results together with their 95 per cent confidence intervals (CIs). A fixed-effect meta-analysis of the combined complications was conducted using RevMan 5.3 systematic review software (Cochrane collaboration, Copenhagen, Denmark), and funnel plots were obtained using Stata 16 statistical analysis software (Stata, College station, USA). All studies were considered to have been conducted under similar conditions with similar interventions and patients. Hence, we assumed the only difference between studies was their ability to detect the outcomes of interest.

The secondary continuous outcomes were the length of in-hospital stay and drain output. Because of the methodological heterogeneity in the included studies, a narrative analysis of the results was performed.

Significance thresholds based on recommendations to improve the use of statistics in biomedicine were defined by p-values of: $p < 0.005$ as significant, $p > 0.05$ as non-significant and $0.005 < p < 0.05$ as suggestive.[10,11]

Assessment of reporting bias

Despite the small number of studies included, funnel plots were constructed to determine whether publication bias was a factor because of the inclusion of grey literature in our analysis.

Results

Search results

In our literature search of Medline for 'drainless or tissue sealant', 38 910 results were obtained, and for 'parotidectomy', 4259 reports were found. Combination of both terms yielded 15 papers. During a similar search on Embase, 48 928 results were obtained for 'drainless or tissue sealant', and 3242 results were obtained for 'parotidectomy'. Combination of both results retrieved 17 papers. Using PubMed, 50 802 results were generated for 'drainless or tissue sealant' and 4 528 258 results for 'parotidectomy', giving a combined result of 15 828. Our final comprehensive search identified 15 860 studies; 15 847 were irrelevant and discarded, and the remaining 13 studies were selected for our review based on the inclusion criteria. Four studies[12–15] were excluded as they did not review the use of tissue sealant in parotidectomy surgery specifically. Of the included studies, four[16–19] did not have any control group and were included in the qualitative synthesis, and the remaining nine studies[4,8,20–26] were quantitatively analysed. The search process performed in June 2020 is detailed in the Preferred Reporting Items for Systematic Review and Meta-analysis ('PRISMA') flow diagram as shown in Figure 1.

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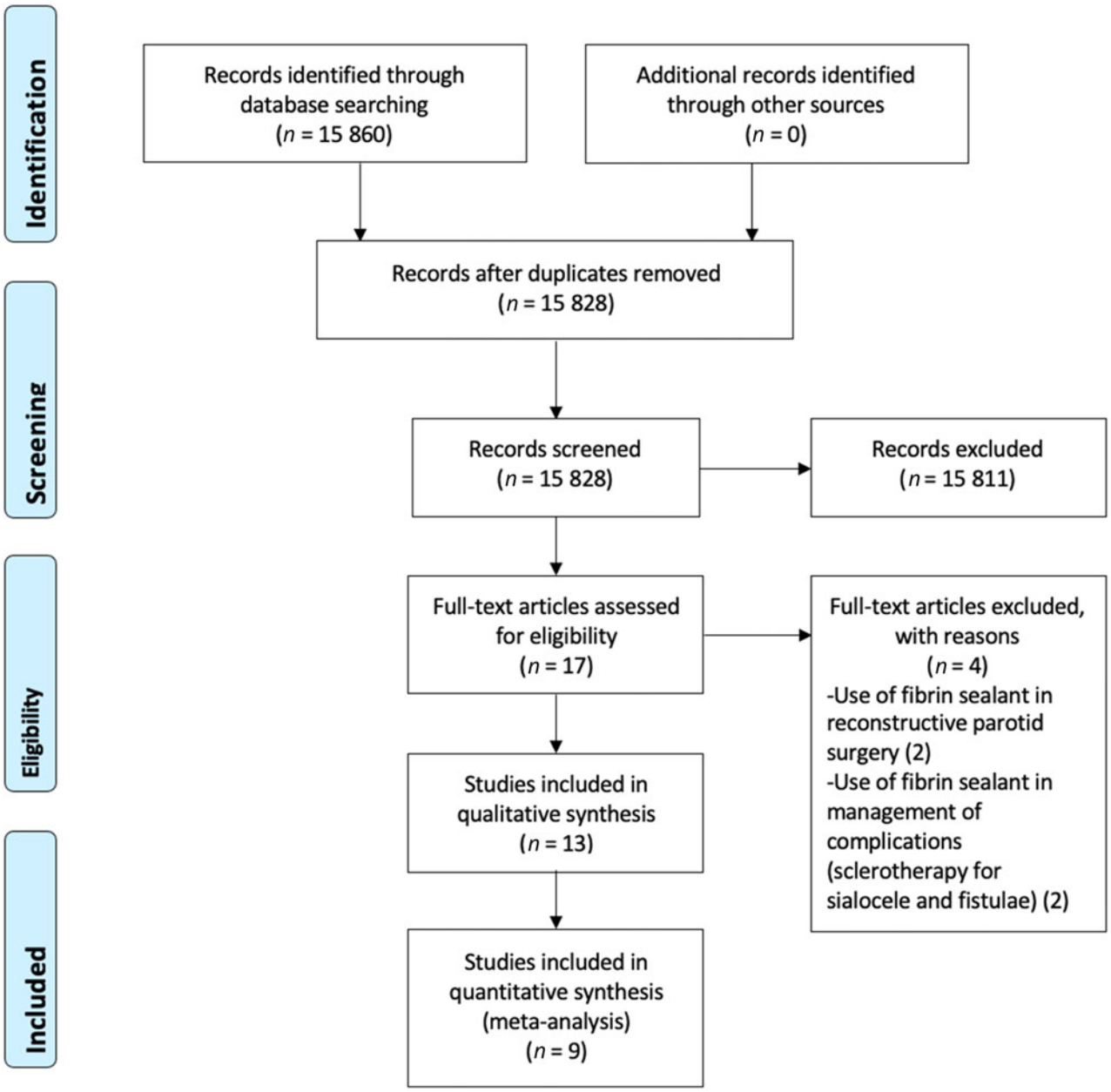

Figure 1. Shows the Preferred Reporting Items for Systematic Review and Meta-analysis ('PRISMA') diagram for the search strategy.

Characteristics of included studies

A total of 642 patients were included in our analysis. Of the 13 selected papers, 7 studies were performed prospectively,[17–21,24,26] and 6 were performed retrospectively.[4,8,16,22,23,25] Four of the studies had no control and only assessed the outcomes of fibrin use in parotidectomy procedures,[16–19] and the remaining nine compared fibrin use with the conventional method.[4,8,20–26] In the study by Patel *et al.*,[8] they assessed three sets of data, the use of absorbable haemostatic agent was not analysed in this paper since we decided to assess fibrin sealants only in drainless cases. Table 1 summarises the main characteristics of the studies.

Methodological quality of included studies

The inclusion of grey literature (unpublished studies in the form of conference abstracts or letters, which might not have been peer-reviewed) minimises publication bias. The argument for the inclusion of grey literature is to fully take into consideration all existing evidence. These studies often include a smaller sample, but excluding them can lead to the exaggeration of statistically significant results, publication bias and skewing the effect size estimates.[27,28] Therefore, Conn *et al.*[28] encouraged the inclusion of grey literature with assessment of heterogeneity. However, because of a lack of methodology details, the papers have been highlighted as high risk of bias as shown in Figure 2. Some papers have not commented on whether participants and outcome assessors have been blinded, and others have not expanded the selection process (as detailed in Appendix 2). Figure 2 provides a summary of the quality of the studies.

Findings

Table 1 summarises how the primary and secondary outcomes post-parotidectomy with tissue sealant compare with conventional methods. It provides a numerical comparison of the length of stay, drain output and complication rates for both.

Figure 3 shows the post-operative complications for procedures using fibrin glue compared with conventional ones.

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Table 1. Characteristics of included studies

Study (author, year)	Sample size	Type of comparative study	Intervention Group					Control Group				
					Outcomes					Outcomes		
			Patients (*n*)	Sealant type	Length of stay	Complications (*n*)	Drain output	Patients (*n*)	Type	Length of stay	Complications (*n*)	Drain output
Studies reporting drainless parotidectomy procedures with fibrin sealant compared with conventional procedures with drains												
– Chudek *et al.* 2020[26]	60	Prospective analysis	29	Fibrin sealant (full thickness skin graft)	Median, 0 days (IQR, 1 day), 25 day-cases	2 seroma/ sialocele	N/A	24	Partial parotidectomy with surgical drain in 24 cases	Median, 2 days (IQR, 2 days), 5 day-cases	8 seroma/ sialocele 1 haematoma	N/A
– Chorney *et al.* 2019[25]	100	Retrospective analysis	46	Fibrin sealant Tisseel with 4 of 46 with passive drains	NR	11 haematoma/ seroma/sialocele	N/A	54	Conventional surgery with drains	NR	9 haematoma/ seroma/ sialocele	N/A
– Cunniffe *et al.* 2019[4]	34	Retrospective analysis	17	Fibrin sealant Artiss	Mean, 0.52 days	2 seroma, 3 salivary leak	N/A	17	Conventional surgery with drains	Mean, 1.64 days	1 seroma, 4 salivary leak	N/A
– Chua 2016[24]	70	Prospective randomised, case control	35	Fibrin sealant Tisseel with pressure bandage	Mean, 1.1 days	3 sialocele	N/A	35	Fibrin sealant Tisseel™ without pressure bandage	Mean, 2.8 days	4 sialocele	N/A
– Too *et al.* 2015[23]	22	Retrospective review	13	Fibrin sealant Artiss	NR	8 post-operative complications	N/A	9	Traditional without Artiss™	NR	6 post-operative complications	N/A
– Depondt *et al.* 1996[22]	68	Retrospective analysis	34	Fibrin sealant Tisseel	15-day cases, 18 two-day admissions	2 salivary fistulae	N/A	34	Conventional suture	34 3-day admissions	5 haematoma, 1 salivary fistula, 4 facial paralysis, 1 flap necrosis	N/A
Studies reporting fibrin sealant use with drains compared with conventional procedures with drains in parotidectomy procedures												
– Heffernan *et al.* 2015[20]	85	Prospective review	42	Fibrin sealant Artiss prior to skin closure (with or without suction drainage)	Median, 1 day	1 haematoma, 1 seroma	Mean drain output, 2 ml	43	Post-operative suction drainage	Median, 4 days	1 haematoma, 2 seroma	Mean drain output, 20 ml
– Patel *et al.* 2006[8]	113 (32 with absorbable haemostatic agent excluded)	Retrospective consecutive study	26	Fibrin sealant Tisseel with drain	Mean, 1.2 days	0 complications	Mean drain output, 15.3 ml	37	Standard wound closure with drain	Mean, 2.8 days	1 seroma	Mean drain output, 27.1 ml
Maharaj *et al.* 2005[21]	50	Prospective randomised, controlled trial	28	Fibrin sealant Tisseel with drain	Mean, 1.4 days	1 seroma	Mean drain output, 41.3 ml	22	Traditional extended stay with drain	Mean, 1.6 days	5 seroma	Mean drain output, 65.3 ml

Studies reporting fibrin sealant use in parotidectomy procedures without any control group										
– Poolovadoo *et al.* 2019[16]	31	Retrospective analysis	31	Fibrin sealant Artiss	27 day-cases, 4 with more than 1-day stay	1 haematoma, 1 poor respiratory reserve	N/A	NR	None	NR	NR	N/A
– Al-Qahtani *et al.* 2011[19]	10	Prospective cohort study	10	Fibrin sealant Tisseel without drain	Median, 1 day	2 facial nerve weaknesses with full recovery	N/A	NR	None	NR	NR	N/A
Trujillo *et al.* 2009[18]	10	Prospective study	10	Fibrin sealant	Median, 2 days	0	N/A	NR	None	NR	NR	N/A
Conboy *et al.* 2008[17]	21	Prospective cohort study	21	Fibrin sealant Tisseel without drain	20 day-cases, 1 overnight admission	0	N/A	NR	None	NR	NR	N/A

N/A = not available; NR = not reported; IQR = interquartile range

Complications rates varied from 2.6 per cent[8] to 61.5 per cent [23] with fibrin use and from 2.3 per cent[8] to 66.7 per cent[23] with conventional surgery. The most common complication was seroma formation, reported by six studies,[4,8,20,21,25,26] followed by haematoma, reported by three studies.[24–26] Other complications reported were salivary leak, salivary fistula, facial paralysis, facial nerve weakness, sialocele, flap necrosis and sepsis.[4,8,22,24–26]

A fixed-effect meta-analysis was carried out over different formulations of fibrin sealants to assess its effectiveness on post-parotidectomy outcomes in terms of complications, as shown in the forest plot of Figure 2.

The findings of this meta-analysis are suggestive of more favourable outcomes in drainless parotidectomy procedures with tissue sealant in comparison with conventional post-operative drain use ($p = 0.04$; odds ratio = 0.57; 95% CI, 0.33 to 0.98) as shown in Figure 2a. With regards to the use of fibrin sealant in conjunction with post-operative drains as compared with drains alone, our analysis has shown a reduction in complications with fibrin sealant use ($p = 0.08$; odds ratio = 0.33; 95% CI, 0.09 to 1.15), as shown in Figure 2b. Because of the variation in the secondary dichotomous outcomes as mentioned above, as well as the disparities in methodologies used, mainly in the grey literature (non-peer reviewed literature), a sub-group meta-analysis was performed, excluding the latter. A similar result of fewer complications was observed following the use of fibrin sealant, which is also suggestive of improved outcomes ($p = 0.04$; odds ratio = 0.55; 95% CI, 0.31 to 0.97) as shown in Figure 2c. Both between- and within-study heterogeneity contributed to variance in our analysis ($I^2 = 23$ per cent; Cochran's Q = 10.43). However, upon filtering out grey literature we note an unchanged variance (Cochran's Q = 10.35) supporting its inclusion in our study, as shown in Figure 4.

Discussion

Our meta-analysis demonstrated favourable outcomes with the use of fibrin sealant compared with parotidectomy with drains, potentially reducing the incidence of post-operative complications. The randomised, controlled trial by Maharaj *et al.*[21] reported similar results with a lower incidence of haematoma and seroma formations with fibrin sealant use. Chua[24] and Heffernan[20] showed a relatively lower rate of complications, with 8.5 per cent and 4.8 per cent, respectively, with the use of fibrin sealant, compared with 11.4 per cent and 6.9 per cent, respectively, in conventional parotidectomy procedures. Other complications included salivary leak, salivary fistula, facial paralysis, sepsis and flap necrosis, reported in the studies by Cunniffe *et al.*[4] and Depondt *et al.*[22] The former had an equal number of complications with both fibrin sealant use and conventional surgery. Similarly, only one seroma formation was reported by Patel *et al.*[8] in both groups.

Complication rates have varied in studies that only reviewed the use of fibrin sealant. Trujillo[18] and Conboy *et al.*[17] had a 0 per cent complication rate in a sample size of 10 and 21 patients, respectively. Poolovadoo *et al.*[16] reported 1 post-operative haematoma and 1 decline in respiratory function (6.5 per cent incidence rate). These are relatively low incidences that might not be fibrin sealant related. The study by Chorney and Ryan,[25] with one of the largest series of patients, found almost similar wound complication rates between the sealant and non-sealant groups when other factors such as tissue volume removed, smoking history, diabetes and

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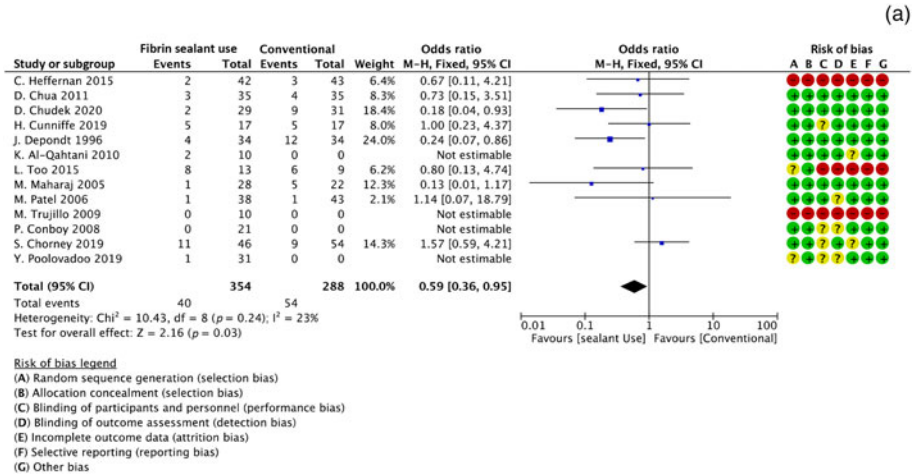

Figure 2. Forest plots and methodological quality analysis for the included studies, showing (a) plot with all included studies and (b) plot excluding grey literature. M-H = Mantel–Haenszel; CI = confidence interval.

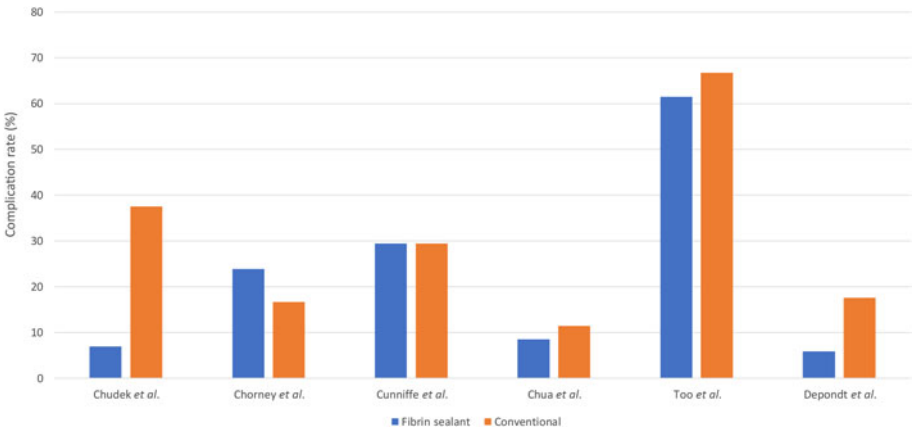

Figure 3. Graph of complication rates between the sealant and non-sealant groups.

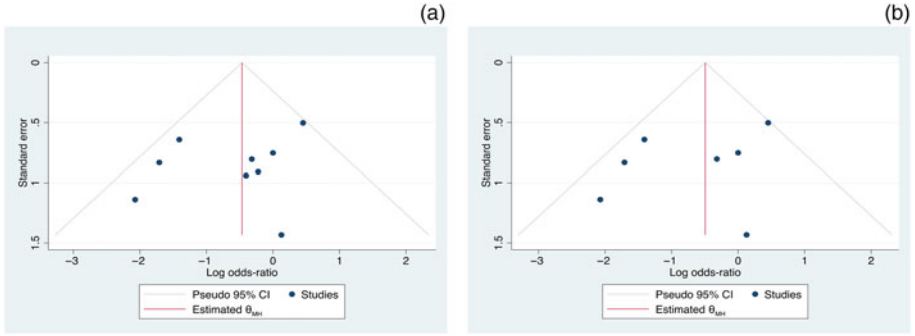

Figure 4. Funnel plots for the included studies, showing (a) all included studies and (b) where grey literature was excluded. The horizontal axis represents the log odds-ratio against the vertical standard error of log odds-ratio. CI = confidence interval; M-H = Mantel–Haenszel.

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anticoagulant use were accounted for. Chudek *et al.*[26] also demonstrated a reduced incidence of seroma and haematoma in the fibrin sealant group, suggesting the use of fibrin sealant as a possible alternative, enabling the omission of surgical drains while also reducing patient discomfort and anxiety associated with these.[4]

Al-Qahtani *et al.*[19] had 2 incidences of facial nerve weaknesses with full recovery out of 10 surgeries performed with fibrin sealant. Although this is a comparatively higher incidence, the sample size is too small draw conclusions. Similarly, Too *et al.*[23] reported a higher number of complications with fibrin sealant, compared with conventional surgery. However, not all complications were Artiss-related, and their sample size was small as well.

One argument for fluid collection leading to seroma and haematoma formation could be due to uneven distribution of the fibrin glue along the parotid bed and lack of manipulation and compression, leading to less adherence.[4] Ensuring a more uniform spread of fibrin glue could potentially improve adherence. Five of the included studies[4,22–24,26] showed a comparative or lower incidence rate of post-parotidectomy complications with fibrin sealant, as shown in Figure 3. Hence, fibrin sealant may be considered as an alternative, enabling the omission of surgical drains while also reducing patient discomfort and anxiety associated with these.[4]

Considering drain output volume, a meta-analysis on fibrin sealant use in head and neck surgery by Bajwa *et al.*[1] showed a reduction in wound drainage volume with fibrin sealant. A similar result was reported by Maharaj *et al.*,[21] Heffernan *et al.*[20] and Trujillo *et al.*[18] with the latter reporting a *p*-value of less than 0.005. Therefore, fibrin sealants may enable drainless surgical procedures, overcoming the pain, distress and discomfort caused by surgical drains.[1]

Cost-effectiveness of a procedure is a crucial part to consider. Length of in-hospital stay is an important contributory factor. Fibrin sealants enable a drainless procedure, meaning most patients can be discharged on the same day. Chua[24] and Patel *et al.*[8] found a reduction in length of hospital stay. The former study showed a mean length of hospital stay of 1.1 days versus 2.8 days whereas the latter study had a length of 1.2 days versus 2.8 days for drainless and conventional parotidectomy, respectively. Nausea control was the main reason for overnight stay in both studies.

In the study by Depondt *et al.*,[22] all patients who had surgery with fibrin sealant were discharged by day 2, while those who underwent conventional surgery were only discharged after day 3 because of complications and drain care. Social aspects can also be a barrier to discharge as shown by Poolovadoo *et al.*,[16] who reported 4 overnight in-hospital stays out of 31 patients, 1 of which was because of lack of support at home. Cunniffe *et al.*[4] stated that 9 out of 17 patients required an overnight stay because of a late afternoon finish in the group with fibrin sealant use, with an average length of stay of 0.52 days compared with 1.64 days in those who had conventional surgery.

The overwhelming majority of patients who underwent parotidectomy with a post-operative drain had two or more days of in-hospital stay. Cost-wise, although fibrin sealant (Artiss in this case) costs £165.75 compared with £30 for a drain per patient as mentioned by Cunniffe *et al.*,[4] an overnight hospital stay cost was £241 on a surgical ward in 2018 to 2019.[29] Therefore, the reduction in length of stay in hospital greatly outweighed the price difference.

Our meta-analysis has several limitations. The included studies are of a very small sample size, and the retrospective nature of some studies[4,8,16,22,23,25] may incorporate selection bias. Participants with drainless parotidectomy for which outcomes were not specified[26] could not be included in our results. Although the inclusion of conference abstracts may contribute to publication bias, our analysis has shown minimal variance when these were excluded. Moreover, Patel *et al.*[8] excluded patients sent home with drains from their analysis, thus conferring attrition bias to the study. The studies using fibrin sealant in conjunction with post-operative drains might be subject to confounding results as proper apposition of skin flaps is not feasible with passive drains.[25] Therefore, there is a requirement for more robust evidence through larger samples and prospective cohort studies to allow broader conclusions to be drawn.

Conclusion

Fibrin sealant in parotidectomy may be used to facilitate a drainless approach, expediting recovery and offering better comfort to patients. Furthermore, patients are candidates for same day discharges, reducing the length of in-hospital stay, saving on costs and resources. Thus, fibrin sealant offers significant advantages over traditional parotidectomy procedures with drain insertion, with comparable safety. The suggested benefits of fibrin sealant presented in our analysis should be further explored through reformed research of more robustly designed studies comparing the use of fibrin sealant without drains to the use of post-parotidectomy drains.

Competing interests. None declared

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Appendix 1. Medical subject heading terms used for the search strategy

((drainless).ti,ab OR (sealant).ti,ab OR (tissue sealant).ti,ab OR (fibrin).ti,ab OR (fibrin sealant).ti,ab) AND ((parotidectomy).ti,ab OR (parotidectomies).ti,ab OR (parotidectomy*).ti,ab OR (parotidectom*).ti,ab OR (post-parotidectomy).ti,ab OR (Postparotidectomy).ti,ab OR (Postparotidectom*).ti,ab OR (Postparotidectomies).ti,ab OR (Post-parotidectomies).ti,ab OR (Parotid surgery).ti,ab OR (Parotid Surgeies).ti,ab OR (Post-parotid surgeries).ti,ab OR (Post-parotid surgery).ti,ab OR (post parotid surgery).ti,ab OR (post parotid surgeries).ti,ab)

Appendix 2. Characteristics and methodological assessment of the included studies

Heffernan 2015[20]

Parameter	Details
Methods	Prospective analysis comparing 42 patients between January 2011 to December 2012 with 43 patients between January 2013 to July 2014
Participants	85 patients in total
Interventions	Use of Artiss prior to skin closure
Outcomes	Shorter length of hospital in-stay
Notes	

Risk of bias table

BIAS	AUTHORS' JUDGEMENT	SUPPORT FOR JUDGEMENT
RANDOM SEQUENCE GENERATION (SELECTION BIAS)	High risk	
ALLOCATION CONCEALMENT (SELECTION BIAS)	High risk	
BLINDING OF PARTICIPANTS AND PERSONNEL (PERFORMANCE BIAS)	High risk	
BLINDING OF OUTCOME ASSESSMENT (DETECTION BIAS)	High risk	
INCOMPLETE OUTCOME DATA (ATTRITION BIAS)	High risk	Only abstract available
SELECTIVE REPORTING (REPORTING BIAS)	High risk	
OTHER BIAS	High risk	Abstract only

Chua 2011[24]

Parameter	Details
Methods	Prospective randomised, case control study
Participants	70 patients
Interventions	Fibrin glue versus drains
Outcomes	Cheaper, shorter stays, less comorbidities
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	
Allocation concealment (selection bias)	Low risk	
Blinding of participants and personnel (performance bias)	Low risk	
Blinding of outcome assessment (detection bias)	Low risk	
Incomplete outcome data (attrition bias)	Low risk	
Selective reporting (reporting bias)	Low risk	
Other bias	Low risk	

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Chudek *et al.* 2020[26]

Parameter	Details
Methods	Retrospective and prospective comparison
Participants	60 patients
Interventions	use of fibrin sealant
Outcomes	2 complications, lower than those without fibrin sealant
Notes	

Risk of bias table

BIAS	AUTHORS' JUDGEMENT	SUPPORT FOR JUDGEMENT
RANDOM SEQUENCE GENERATION (SELECTION BIAS)	Low risk	Retrospective and prospective comparison
ALLOCATION CONCEALMENT (SELECTION BIAS)	Low risk	
BLINDING OF PARTICIPANTS AND PERSONNEL (PERFORMANCE BIAS)	Low risk	
BLINDING OF OUTCOME ASSESSMENT (DETECTION BIAS)	Low risk	
INCOMPLETE OUTCOME DATA (ATTRITION BIAS)	Low risk	
SELECTIVE REPORTING (REPORTING BIAS)	Low risk	
OTHER BIAS	Low risk	

Cunniffe *et al.* 2019[4]

Parameter	Details
Methods	Retrospective
Participants	34 patients
Interventions	Use of Artiss versus conventional surgical drains
Outcomes	Shortened hospital stay
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	
Allocation concealment (selection bias)	Low risk	
Blinding of participants and personnel (performance bias)	Unclear risk	No other changes in technique, instrumentation or procedure was made
Blinding of outcome assessment (detection bias)	Low risk	Patients were assessed similarly
Incomplete outcome data (attrition bias)	Low risk	
Selective reporting (reporting bias)	Low risk	
Other bias	Low risk	

Depondt *et al.* 1996[22]

Parameter	Details
Methods	Retrospective comparison
Participants	68 patients
Interventions	Drain insertion versus fibrin use
Outcomes	Reduction in post-operative complications and length of stay
Notes	

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Risk of bias table

BIAS	AUTHORS' JUDGEMENT	SUPPORT FOR JUDGEMENT
RANDOM SEQUENCE GENERATION (SELECTION BIAS)	Low risk	Random
ALLOCATION CONCEALMENT (SELECTION BIAS)	Low risk	
BLINDING OF PARTICIPANTS AND PERSONNEL (PERFORMANCE BIAS)	Low risk	No mention of risk
BLINDING OF OUTCOME ASSESSMENT (DETECTION BIAS)	Low risk	
INCOMPLETE OUTCOME DATA (ATTRITION BIAS)	Low risk	
SELECTIVE REPORTING (REPORTING BIAS)	Low risk	
OTHER BIAS	Low risk	

Al-Qahtani 2010[19]

Parameter	Details
Methods	Prospective Study
Participants	10 patients
Interventions	Tisseel without drain
Outcomes	Short length of stay, few complications
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Consecutive
Allocation concealment (selection bias)	Low risk	
Blinding of participants and personnel (performance bias)	Low risk	
Blinding of outcome assessment (detection bias)	Low risk	
Incomplete outcome data (attrition bias)	Unclear risk	None mentioned
Selective reporting (reporting bias)	Low risk	
Other bias	Low risk	

Too and Nugent 2015[23]

Parameter	Details
Methods	Retrospective study
Participants	22 patients
Interventions	Artiss use versus control
Outcomes	Shortened hospital stay
Notes	Conference abstract

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Unclear selection process
Allocation concealment (selection bias)	Low risk	
Blinding of participants and personnel (performance bias)	High risk	No blinding mentioned
Blinding of outcome assessment (detection bias)	High risk	
Incomplete outcome data (attrition bias)	High risk	Unknown
Selective reporting (reporting bias)	High risk	
Other bias	High risk	Grey literature with little methodology evidence

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Maharaj *et al.* 2005[21]

Parameter	Details
Methods	Randomised, control trial
Participants	50 patients
Interventions	The use of Tisseel versus standard model
Outcomes	Tisseel use was associated with less drain output and fewer complications; length of stay had no statistical difference
Notes	Very well performed study

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Sealed envelopes used
Allocation concealment (selection bias)	Low risk	Sealed envelopes used
Blinding of participants and personnel (performance bias)	Low risk	Blinded correctly
Blinding of outcome assessment (detection bias)	Low risk	Outcome assessors were blinded as well
Incomplete outcome data (attrition bias)	Low risk	Only completed data was included
Selective reporting (reporting bias)	Low risk	Transparency
Other bias	Low risk	Good study with minimal risk of bias

Patel *et al.* 2006[8]

Parameter	Details
Methods	Retrospective data collection
Participants	81 patients
Interventions	Use of fibrin sealant against standard method (68 per cent of patients with fibrin sealant had drain insertion compared with 93 per cent of those with the standard method of haemostasis)
Outcomes	Fibrin sealant was associated with less drains, earlier drain removals, shorter lengths of stay and less complications
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Consecutive data collection
Allocation concealment (selection bias)	Low risk	None
Blinding of participants and personnel (performance bias)	Low risk	Retrospective and consecutive data collection
Blinding of outcome assessment (detection bias)	Unclear risk	Not clear
Incomplete outcome data (attrition bias)	Low risk	Incomplete data excluded
Selective reporting (reporting bias)	Low risk	None
Other bias	Low risk	

Trujillo 2009

Parameter	Details
Methods	Prospective study
Participants	10 patients
Interventions	Fibrin sealant with vacuum drains
Outcomes	Less drain output, shorter length of stay
Notes	Conference abstract

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Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	
Allocation concealment (selection bias)	High risk	
Blinding of participants and personnel (performance bias)	High risk	
Blinding of outcome assessment (detection bias)	High risk	
Incomplete outcome data (attrition bias)	High risk	
Selective reporting (reporting bias)	High risk	
Other bias	High risk	Abstract without much detail about methodology

Conboy *et al.* 2008[17]

Parameter	Details
Methods	Prospective study
Participants	21 patients
Interventions	Evaluating day surgery with fibrin sealant and without drain
Outcomes	Only 1 admission and no complication
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Consecutive patients
Allocation concealment (selection bias)	Low risk	
Blinding of participants and personnel (performance bias)	Unclear risk	No mention
Blinding of outcome assessment (detection bias)	Unclear risk	No mention
Incomplete outcome data (attrition bias)	Low risk	All included
Selective reporting (reporting bias)	Low risk	None
Other bias	Low risk	

Chorney and Ryan 2019[25]

Parameter	Details
Methods	Retrospective
Participants	100 patients
Interventions	Fibrin sealant
Outcomes	24 per cent had seroma or haematoma
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Consecutive
Allocation concealment (selection bias)	Low risk	
Blinding of participants and personnel (performance bias)	Unclear risk	Retrospective nature, not specified any blinding in methodology
Blinding of outcome assessment (detection bias)	Low risk	
Incomplete outcome data (attrition bias)	Unclear risk	No mention
Selective reporting (reporting bias)	Low risk	
Other bias	Low risk	

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Poolovadoo *et al.* 2019[16]

Parameter	Details
Methods	Retrospective
Participants	31 patients
Interventions	Use of Artiss
Outcomes	1 complication, 4 overnight admissions
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	There was a gender and age imbalance
Allocation concealment (selection bias)	Low risk	
Blinding of participants and personnel (performance bias)	Unclear risk	No mention of blinding, hence risk cannot be commented on
Blinding of outcome assessment (detection bias)	Unclear risk	Due to the retrospective nature, it cannot be commented on
Incomplete outcome data (attrition bias)	Low risk	
Selective reporting (reporting bias)	Low risk	
Other bias	Low risk	

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