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Review Article

Fibrin Sealants in Neurosurgery: A Structured Literature Review of Efficacy and Complications

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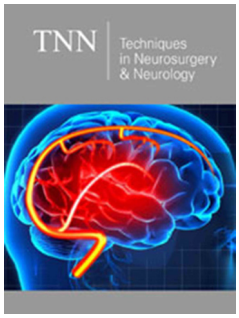

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Abstract

Objective: Fibrin sealants have become integral in neurosurgical practice, offering both hemostatic and tissue-sealing benefits across diverse intracranial procedures. Despite widespread use, evidence regarding their efficacy and safety remains inconsistent. This review aims to synthesize current applications, outcomes and reported complications in intracranial neurosurgery.

Methods: A narrative literature review with systematic search methods was conducted in accordance with key PRISMA 2020 principles. PubMed database was searched from inception using combinations of MeSH terms and keywords related to "fibrin sealant," "neurosurgery," "intracranial hemostasis" and "dural closure." Eligible studies included Randomized Controlled Trials (RCTs), cohort studies, case series and reviews reporting clinical outcomes of fibrin sealant use in intracranial procedures. Data were extracted regarding application type, efficacy and complications. Due to heterogeneity among studies, results were synthesized narratively.

Results: A total of 22 studies met the inclusion criteria. Fibrin sealants were useful for dural closure, reduction of Cerebrospinal Fluid (CSF) leakage and hemostasis during tumor and vascular surgeries. Meta-analyses revealed inconsistent results on preventing postoperative CSF leaks, with some reporting benefit and others no difference from standard closure. In skull base and vascular procedures, sealants improved operative visualization and decreased bleeding. Reported complications included postoperative mass effect, adhesion formation, inflammation and allergic or thromboembolic events.

Conclusion: Fibrin sealants remain valuable adjuncts in neurosurgery, enhancing hemostasis and facilitating watertight dural closure. However, variability in formulation and expansion properties can lead to rare but severe complications. Current evidence is based on small series and heterogeneous studies, underscoring the need for high-quality RCTs to establish guidelines for their safe and effective use.

Keywords: Cerebrospinal fluid; Complications; Fibrin sealants; Hemostatic agents; Neurosurgery

Abbreviations: CSF: Cerebrospinal Fluid; RCTs: Randomized Controlled Trials; MVD: Microvascular Decompression; DESS: DuraSeal Exact Spine Sealant

Introduction

Intracranial neurosurgery presents remarkable challenges due to the risk of Cerebrospinal Fluid (CSF) leakage, the complex anatomy and the need for hemostasis. Over decades, various hemostatic agents have been developed to address these unique challenges [1]. Among these hemostatic agents, fibrin sealants have emerged as particularly valuable tools in the neurosurgical armamentarium. These biologically derived products, provide effective hemostasis while offering additional benefits as tissue sealants [2]. Fibrin sealants demonstrate remarkable versatility across neurosurgical applications, including: Dural closure, hemostasis during tumor resection and controlling venous bleeding [3]. Despite their widespread adoption and generally favorable safety profile, neurosurgeons must maintain awareness of potential adverse events associated with these products [4]. Unfortunately, current literature provides limited evidence regarding both the efficacy and potential adverse

effects of fibrin sealants in intracranial procedures. Fibrin sealants function through a biomimetic mechanism that replicates the final stages of the physiological coagulation cascade. In this process, human fibrinogen is converted to fibrin monomers by thrombin and the resultant fibrin strands are cross-linked by factor XIIIa to form a stable clot that mimics physiological hemostasis [5]. The fibrin matrix formed serves as both a physical barrier to blood loss and a scaffold for cell migration during wound healing. Other specialized variants like integrate the fibrin components into collagen sheets to enhance handling characteristics and facilitate targeted application in neurosurgical procedures [1-3]. Neurosurgeons have adapted these sealants for various applications, including dural closure, embolization procedures, microvascular decompression, transsphenoidal surgery and peripheral nerve repair [2,3]. Among these, the strategic injection of fibrin sealant into cavernous sinus compartments represents a transformative technique in skull base surgery. This technique effectively controls venous oozing from this challenging region and facilitates safer access to deep-seated pathologies minimizing the risk of nerve injury [3]. Moreover, sealants can be used in endovascular embolization for Arteriovenous Malformations (AVM), arteriovenous fistulas and aneurysms [2-6]. However, their use is associated with potential complications, including tissue ischemia, hemorrhage and catheter adhesion [6]. Therefore, this study aimed to investigate the role of fibrin sealants in intracranial neurosurgery, with a particular focus on their efficacy and associated complications.

Methods

Literature search strategy

A narrative literature review with systematic search methods was conducted in accordance with key PRISMA 2020 principles and a PRISMA flow diagram was prepared. The primary objective was to evaluate the role of fibrin sealants and bio adhesives in neurosurgical intracranial procedures. The study selection process is illustrated in the PRISMA flow diagram. A structured search was performed in PubMed up to May 27, 2025. PubMed database was searched from inception using combinations of MeSH terms and keywords related to "fibrin sealant," "neurosurgery," "intracranial hemostasis" and "dural closure.". Boolean operators (AND/OR) were used to refine the search. Additionally, reference lists of relevant articles were screened to identify supplementary studies.

Study selection and eligibility criteria

Studies were included based on predefined inclusion and exclusion criteria. Eligible studies met the following criteria: [1] investigated the use of fibrin sealants in intracranial hemostasis or dural closure, [2] reported clinical or surgical outcomes and [3] were Randomized Controlled Trials (RCTs), cohort studies, reviews or case series. Studies focusing solely on animal models or non-surgical interventions were excluded, as well as non-English publications and studies lacking clear patient outcomes. Screening was performed in two phases: Title and abstract screening, followed by full-text review. After applying the inclusion criteria and quality assessment, 11 studies were considered eligible. An additional 11 studies were identified through backward citation analysis, bringing the total number of included studies to 22. A PRISMA-style flow diagram (Figure 1) summarizes the selection process.

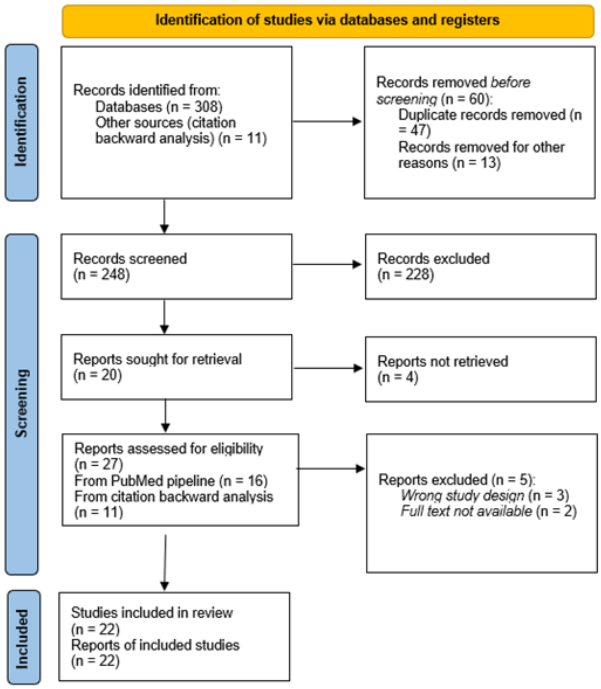

Figure 1: PRISMA 2020 flow diagram illustrating the study selection process.

Data extraction and quality assessment

Two independent reviewers (FR, MC) screened articles and extracted data regarding clinical applications, surgical outcomes, efficacy in intracranial hemostasis and reported complications such as sealant expansion, CSF leak, adhesion formation and inflammatory responses. Any discrepancies were resolved through discussion and consensus.

Data synthesis

A narrative synthesis approach was used to summarize the findings from the included studies. Key themes were identified, including patient selection criteria, hemostatic product used, surgical interventions and clinical outcomes. Given the anticipated heterogeneity in study design and outcome reporting, a formal meta-analysis was not performed.

Risk of bias

Since the primary objective of this review was to provide a broad synthesis of the available evidence rather than to critically appraise study quality, a formal risk of bias assessment was not performed. The findings should therefore be interpreted as a narrative synthesis informed by systematic search methods.

Results

We identified 22 articles examining the application of fibrin sealants in intracranial neurosurgery, with particular attention to their efficacy and reported complications (Table 1).

Table 1: Summary of included studies.

Author (Year)	Country/ Setting	Study Design	N Studies/P*	N patients	Bioadhesive (Type/ Product)	Comparator (if any)	Key Findings	Notes
Giammalva et al. [1]	Italy	SR†	7488 studies	Not reported	Tisseel, Vivostat	Sutures alone	Review of hemostatic methods	QA‡
Qiu et al. [2]	Singapore	SR	168 studies	Not reported	Tisseel, Evicel, TachoSil, Cyanoacrilate, Duraseal, Bioglue	Sutures alone	Bioadhesives use is prevalent in neurosurgery. Consider their limitations	QA
Krayenbühl et al. [3]	USA	CS§, T¶	217 procedures	217	Fibrin glue	Not reported	Effective in cavernous sinus surgery	Retrospective
Mankadet al. [4]	United Kingdom	LR††	43 studies	Not reported	Fibrin sealants	Sutures alone	Improved time to hemostasis	QA
Jackson [5]	USA	LR	59 studies	Not reported	Fibrin sealants	Sutures alone	Improved time to hemostasis	QA
Hill et al. [6]	USA	LR	10 studies	Not reported	N-butyl cyanoacrylate	Not reported	Embolization is unpredictable	QA
Kinaci et al. [7]	Netherlands	SR	20 studies / 3682 P	2321	Fibrin sealants	Sutures alone	↓ Risk of surgical site infection	QA
Esposito et al. [8]	Italy	SR	33 studies	Not reported	Fibrin sealants	Sutures alone	Further RCTs are needed	QA
Sekhar et al. [10]	USA	SR	14 studies	Not reported	Dural substitutes and sealants	Not reported	Adjuncts to reinforce dural repair	QA
Biscola et al. [11]	Brazil	SR	137 studies	Not reported	Fibrin sealants, new bioproduct	Sutures alone	Useful in nervous system repair	QA
Gazzeri et al. [12]	Italy, Spain	CS	97 procedures	97	Evicel	Sutures alone	Effective for venous bleeding control	Retrospective, multi-center
Lee et al. [13]	Korea	CS, T	42 procedures	42	Bioglue-coated Teflon sling	Not reported	Useful in microvascular decompression	Retrospective
Ledezma et al. [14]	USA	CS	295 procedures	169	N-butyl cyanoacrylate	Not reported	90.5% patients had excellent or good outcomes after AVM embolization	Retrospective, single-center, non-randomized
Lauvin et al. [15]	France	CR††	2 procedures	2	BioGlue	Not reported	Delayed cauda equina compression after spinal dural repair	Limited generalizability
Kim et al. [16]	USA	P-NRCS‡‡	924 procedures	924	DuraSeal Exact Spine Sealant System (DESS)	Alternative adjuncts	DESS is safe when compared to alternatives for spinal dural repair	Prospective, multi-center (36 centers)
Carretta et al. [17]	USA	RCS§§, SR	8 studies / 662 P	662	TachoSil	Sutures alone	Safe but without clear advantage in complication avoidance or outcome	Single-institution RC
Auricchio et al. [18]	Italy	RCS	225 studies	225	TachoSil	HydroSet	No significant reduction in CSF leakage	Retrospective
Sivakumar et al. [19]	United Kingdom	RCT¶¶	40 procedures	40	Evicel	Sutures alone	Reduced postoperative CSF leakage and surgical site complications	Multi-center, pediatric subjects

Mosteiro et al. [20]	Spain	LR	142 studies	Not reported	Not reported	Not reported	Glioblastoma multiforme microvasculature may challenge hemostasis	QA
Epstein [21]	USA	P-NRCS	39 procedures	39	Tisseel	Control	Improved time to hemostasis	Prospective, single-center, non-randomized
Yu et al. [22]	China	RCT	200 procedures	200	Bioseal	Sutures alone	Significant reduction in CSF leakage	Prospective, multi-center, Single-blinded

Abbreviations: *P: Patients; †SR: Systematic Review; ‡QA: Qualitative Analysis; §CS: Case Series; ¶T: Technical Note; **LR: Literature Review; ††CR: Case Report; ‡‡P-NRCS: Prospective Non-Randomized Clinical Study; §§RCS: Retrospective Cohort Study; ¶¶RCT: Randomized Controlled Trial

Applications of fibrin sealants in neurosurgery

Dural closure and prevention of cerebrospinal fluid leakage: Sealants have been extensively utilized in neurosurgery to facilitate dural closure and prevent cerebrospinal fluid leakage [7]. A systematic review encompassing 33 studies (2,935 patients) demonstrated that fibrin sealants significantly reduce the incidence of CSF leakage postoperatively [8,9]. However, one meta-analysis of 20 studies involving 3,682 patients found no statistically significant reduction in CSF leakage rates compared to traditional closure methods such as synthetic sealants, collagen or gelatin-based sponges [7]. Fibrin sealants remain a widely adopted adjunct in dural repair, especially in cases of high-risk leaks following tumor resection or neurotrauma [10].

Hemostasis in tumor and vascular neurosurgery: Fibrin sealants can be used as hemostatic agents following the total or partial resection of brain tumors replacing conventional sutures [11]. In a series of 217 cases involving meningiomas, schwannomas, pituitary adenomas, paraclinoid aneurysms and complex basilar aneurysms, fibrin sealants were injected in anatomical "windows" of the cavernous sinus to achieve intraoperative hemostasis. This technique achieved a drier surgical field without any observed clinical complications during postoperative follow-up. Furthermore, postoperative angiographic evaluation demonstrated reestablishment of venous flow within the cavernous sinus within two to three months [3]. In addition, Gazzeri R et al. [12] demonstrated that no patients that were treated with EVICEL to control venous bleeding in cranial procedures needed additional hemostatic procedures [12].

Microvascular decompression in trigeminal neuralgia and hemifacial spasm: A prospective study involving 42 patients undergoing Micro Vascular Decompression (MVD) for hemifacial spasm demonstrated that transposition of the vertebral artery using a fibrin sealant-coated Teflon sling is a safe and effective approach [13]. No symptom recurrence was observed in any cases during a two-year follow-up [13].

Endovascular neurosurgery and embolization procedures: Fibrin sealants are also utilized in endovascular neurosurgery, particularly in the embolization of arteriovenous malformations and other intracranial vascular lesions. A meta-analysis of 295 embolization procedures revealed that fibrin-based adhesives offer superior adhesion properties and biocompatibility compared to other embolic agents. However, those procedures were associated with a higher risk of venous infarction and hemorrhage, especially in complex, high-flow lesions [14].

Adverse events of fibrin sealants: Despite not being a fibrin sealant, DuraSeal has been associated with postoperative volume expansion, a phenomenon that may contribute to parenchymal tissue compression [2,15,16]. This issue prompted the development of a low-swell formulation of DuraSeal. A nonrandomized multicenter study found that the original DuraSeal formulation expanded 38% more than its low-swell counterpart, DuraSeal Exact Spine Sealant (DESS), which exhibited an expansion rate of 19% [16]. Carretta A et al. [17]. in a study that encompassed 662 patients and a systematic review, concluded that the routine use of TachoSil and similar sealants adjunctive to primary duraplasty is generally safe [17]. However, a retrospective review of 225 patients who underwent retrosigmoid craniotomy revealed that TachoSil did not significantly reduce CSF leakage rates [18]. Complications associated with fibrin adhesives include air embolism, cranial nerve compression, infection, systemic allergic reactions and even the formation of de novo aneurysms [15-18]. On the other hand, a multicenter prospective trial in pediatric population undergoing cranial neurosurgical procedures revealed that Evicel (a fibrin sealant) was safe and effective as a primary suture adjunct in this population [19]. Finally, in a systematic review of 28 studies, Esposito et al. [8,9] reported that dural sealants demonstrated no adverse events across the reviewed articles [8,9].

Discussion

This study is, to the best of our knowledge, the first structured literature review to highlight the safety, effectiveness and potential complications associated with the use of fibrin sealants in intracranial neurosurgery. Fibrin sealants are integral to hemostasis in neurosurgical tumor resection, particularly in highly vascularized tumors and structures, where conventional techniques may be insufficient [12] While they are effective in controlling venous bleeding and improving surgical visualization, their use is not devoid of potential adverse effects. Complications such as air embolism and cranial nerve compression have been

reported. What is more, glioblastoma multiforme and other highly vascularized tumors create a microenvironment that necessitates the use of fibrin sealants for hemostasis [20]. Beyond cranial surgery, fibrin sealants such as Tisseel have demonstrated benefits in spine surgery, reducing postoperative drain duration and hospital stay [21]. These findings evidence the need for fibrin sealants when seeking hemostasis but also a measured approach to their application, optimizing its hemostatic advantages while mitigating the risk of adverse outcomes. The nuanced application of fibrin sealants in neurosurgery could be re-examined. While their role in dural repair, hemostasis and even vascular procedures is well documented across systematic reviews and case series, the heterogeneity in outcomes and occasional complication profiles caution against uncritical adoption [7,9-14,17,20]. As demonstrated in prior studies, sealant efficacy is not absolute and variability in formulation, expansion properties and tissue interaction can influence outcomes in ways not always predictable [2,8,22]. In this context, this review serves as a reflection of the complexity that underpins clinical decision-making, reinforcing the need for tailored application, formulation-specific vigilance and continued investigation through prospective, controlled studies. There is a critical need for further refinement in bio adhesive technologies to enhance patient safety in neurosurgical practice. While fibrin sealants remain integral to intraoperative hemostasis and dural closure, variability in composition and performance may influence clinical outcomes. Alternative bio adhesives present a potential avenue for improving both efficacy and safety [2,8,9,22]. Sealants such as DuraSeal, although not fibrin-based, have been associated with postoperative volume expansion, a phenomenon that may contribute to parenchymal tissue compression [2,15,16]. This concern led to the development of a low-swell formulation of DuraSeal. Given the reliance on these agents in neurosurgical procedures, rigorous investigation through controlled studies and clinical trials is imperative to establish standardized, evidence-based guidelines for their optimal use.

A recent meta-analysis demonstrated that the use of dural sealants in cranial neurosurgery reduced postoperative CSF leaks and overall infection rate after craniectomy procedures [23]. Therefore, the effectiveness of fibrin sealants is highly dependent on their careful application, appropriate patient selection and a heightened awareness of potential adverse events. Surgeons must balance the advantages of bio adhesives with the inherent risks, particularly when working in confined anatomical spaces. There remains a scarcity in large-scale randomized controlled trials that compare different bio adhesive formulations. Much of the available data is derived from case series and retrospective reviews, underscoring the need for well-designed studies to establish standardized guidelines. Finally, further research is warranted to evaluate the long-term safety, biomechanical properties and potential advantages of emerging alternatives in neurosurgical applications. This study has several limitations. First, the quality and heterogeneity of the included studies may have influenced the findings, as some lacked randomized controlled designs or long-term follow-up. Second, by limiting our search to PubMed, we may have missed studies indexed only in other databases. However, given the substantial overlap, we considered PubMed sufficient for the focused scope of this review. Third, the evidence supporting the use of fibrin sealants in intracranial neurosurgery remains limited, with conflicting data regarding their effectiveness in reducing CSF leakage and achieving hemostasis in complex vascular structures. Finally, complications such as adhesion formation, thromboembolic events and mass effect due to sealant expansion require further investigation, as current reports are largely anecdotal or based on small case series. Future high-quality clinical trials are needed to better define the safety profile and long-term outcomes associated with fibrin sealant use in neurosurgery.

Conclusion

In conclusion, while fibrin sealants play a crucial role in promoting hemostasis and minimizing complications such as CSF leakage and infection, they must be used carefully. Nevertheless, when applied strategically, fibrin-based adhesives can contribute to improved surgical efficiency and better long-term outcomes. Further research is essential to resolve the existing uncertainties surrounding their efficacy, refine their application in complex neurosurgical procedures and ultimately enhance patient safety.

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Conflict of Interest

None.

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