European Journal of Medical Research

RESEARCH Open Access

Topical tranexamic acid prevents scar tissue formation following craniectomy in a rat model

Ömer Şahin[1*], Tuncer Taşcıoğlu[2], Ayşegül Fırat[3], Hüseyin Selçuk Sürücü[4] and Muzaffer Çaydere[5]

Abstract

Background We carried out a study to assess the efficacy of tranexamic acid in preventing scar tissue in the craniectomy area in rats.

Method Our study consisted of control and tranexamic acid groups with 10 subjects each. All subjects underwent bilateral frontoparietal craniectomy. After craniectomy, cotton pads were applied to the surgical sites. In the controls, the pads were soaked with saline and in the tranexamic acid group the pads were soaked with 30 mg/kg tranexamic acid. Rats were decapitated 30 days after surgery. The degree of scar formation was evaluated pathologically and by electron microscopy. In pathologic evaluation, dura mater thickness, scar tissue density, and arachnoid involvement were evaluated.

Results The outcomes demonstrated that no adhesions were present in the rats of the Tranexamic acid group, whereas the control group exhibited severe scar tissue [eight of ten rats (80%)] with adhesions. Additionally, comparison between the two groups showed that the dura mater thickness of tranexamic acid animals was thinner than that of the control group animals. Similarly, the intensity of scar tissue density and the intensity of arachnoid involvement were much better than the control group.

Conclusions Scar tissue formation following craniectomies represents a significant adverse outcome that may lead to various complications. Intraoperative topical application of tranexamic acid has demonstrated potential efficacy in preventing scar formation in the craniectomy region in rat models.

Keywords Tranexamic acid, Epidural fibrosis, Rat, Craniectomy

Introduction

Adhesions developing between the temporalis muscle and the dura mater following craniectomies may result in dura mater defects, cerebrospinal fluid leakage, and brain parenchymal injuries, which are the most important factors affecting surgical success. There is currently no effective medical or surgical application that has been clinically used to prevent the development of these fibrotic adhesions [16].

Tranexamic acid, a molecule similar to lysine, functions to inhibit fibrinolysis by preventing plasminogen from adhering to fibrin. Due to this feature, it is used to stop bleeding during surgery [9]. Initially, using fibrin to prevent adhesions may seem like a futile effort. However, this concept is supported by numerous studies involving

*Correspondence:
Ömer Şahin
dromersahin060@gmail.com
[1] Department of Neurosurgery, Bestepe State Hospital, 06560 Ankara, Turkey
[2] Department of Neurosurgery, University of Health Sciences, Ankara Training and Research Hospital, Ankara, Turkey
[3] Department of Anatomy, Hacettepe University Faculty of Medicine, Ankara 06100, Turkey
[4] Department of Anatomy, Koç University Faculty of Medicine, Istanbul 34450, Turkey
[5] Department of Pathology, University of Health Sciences, Ankara Training and Research Hospital, Ankara, Turkey

fibrin-derived materials in both animal and human subjects [5]. Bovine-derived aprotinin is a component of several commercial products, including Trasylol® (Nordic), Tisseel (Baxter), and Aprotinin Injection BP (Nordic). Studies by Kurt et al. have demonstrated Aprotinin efficacy in reducing adhesion formation, particularly in preventing peridural fibrosis and dural adhesions following laminectomy [19]. However, since the use of bovine materials is not safe, different fibrinolytic inhibitors are used at present [6]. In the literature, only one study has used tranexamic acid to prevent epidural adhesions [5]. Given its antifibrotic properties, we hypothesized that the local application of tranexamic acid would reduce fibrotic adhesion and dural thickening after craniectomy.

Our study aimed to evaluate the effectiveness of locally applied tranexamic acid in rats that underwent surgical craniectomy.

Materials and methods

Animal population

All experimental procedures in this study adhered to the European Communities Council Directive of 24 November 1986 (86/609/EEC) on the protection of animals used for scientific purposes. Proper care and ethical guidelines were followed at all stages of the research. All the experimental procedures used in this investigation were reviewed and approved by the ethical committee of the Ankara Education and Research Hospital Animal Laboratory. (Ethics Committee Approval Number: 775, Date: 2024.05.22). A licensed veterinarian supervised the procedures to ensure compliance with animal welfare standards. The study utilized 20 male Wistar rats, each approximately 12 months old and weighing an average of 350 g. The rats were anesthetized with intramuscular injection of a combination of ketamine hydrochloride (35 mg/kg; Ketalar; Pfizer, Istanbul, Turkey) and xylazine (10 mg/kg; Rompun; Bayer, Istanbul, Turkey). A single surgeon performed all procedures.

Surgical procedure

Prior to surgery, the rats' frontal regions were shaved, and the surgical area was disinfected using povidone (Batticon; Adeka Pharmaceuticals, Istanbul, Turkey). The rats were then fixated on a board in a prone position. A drill system (MEDTRONIC Midas REX Legend EHS EM100) was employed to perform bilateral frontoparietal craniectomies, measuring 7 to 8 mm. The dura mater was revealed but kept intact. In this comparative study, rats were allocated to two experimental groups. As all animals possessed identical characteristics, randomization was not necessary for the group assignment process.

Control group (n: 10): Saline (Eczacıbaşı-Baxter, Istanbul-Turkey) soaked cotton pads (0.5×0.5 cm) were applied to the dura mater for 5 min.

Tranexamic acid group (n: 10): Cotton pads (0.5×0.5 cm) saturated with 30 mg/kg tranexamic acid (Herajit; Vem, Ankara, Turkey) were placed on the dura mater for 5 min [5].

All the subjects exhibited satisfactory postoperative recovery without neurological deficits. Each rat was provided with a standard diet and maintained under identical conditions. The animals were euthanized using 100 mg/kg of ketamine hydrochloride (Ketalar; Pfizer) 30 days after the operation.

The cranial bones, including the scalp, were extracted as a single unit. After dividing from the midline, one hemisphere was submerged in 10% buffered formalin. The other side was immediately put into 2.5% glutaraldehyde for fixation for 48 h and then postfixed with OsO3.

Evaluation of scar tissue formation

Decalcification, dehydration, and paraffin blocking were performed before the pathological examination. Sections were taken axially at 5 µm thickness. The preparations were stained with haematoxylin and eosin (H&E) and Masson's trichrome. The sections were evaluated by a pathologist unaware of the group formation. Dura mater thickness, scar tissue density, and arachnoid involvement were evaluated in the pathological evaluation. For dura mater thickness, the average of measurements taken from four random points was used [3].

Scar tissue was evaluated using the grading system of He et al.: Grade 0 indicates no scar tissue, Grade I: Thin fibrous band(s) between fibrous tissue and dura mater; Grade II: Adhesions in less than 2/3 of the laminectomy defect; Grade III: Extensive fibrous tissue, adhesions more than 2/3 of the laminectomy defect and/or fibrous tissue reaching the nerve roots [14]. Arachnoid involvement was categorized as present/absent [3].

Table 1 Dura mater thickness measurements of tranexamic acid and the control groups (Values are presented as the median scores (interquartile range))

	Control group	Tranexamic acid group	
Dura mater thickness measurements	40.76 (32.06–51.87) µm	17.78 (13.74–25.6) µm	$p=0.001$

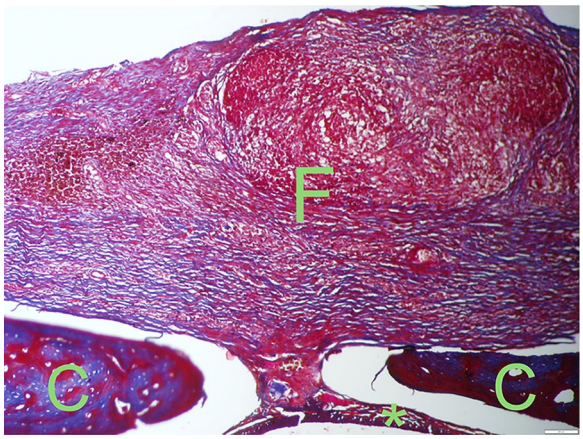

Fig. 1 Control group pathological evaluation shows Grade 3 fibrosis. *C* cranium, *F* fibrosis, *Asterix* dura mater. Masson trichrome

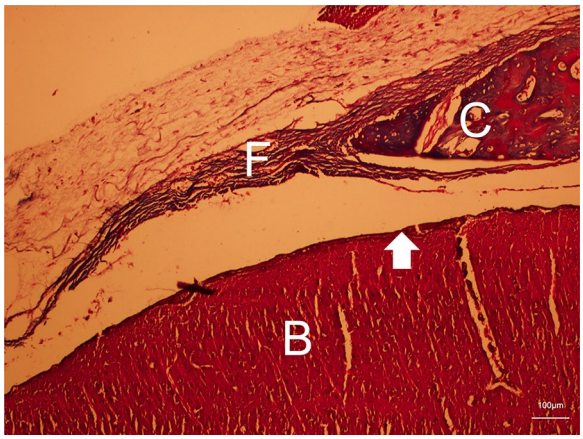

Fig. 2 Tranexamic acid group pathological evaluation shows Grade 1 fibrosis. There wasn't any direct contact among the underlying dura mater with the fibrotic tissue. *C* cranium, *F* fibrosis, *B* brain, *White arrow* dura mater. Masson trichrome

Evaluation using transmission electron microscopy (TEM)

Post fixation samples were dehydrated in a graded series of alcohol solutions and embedded in Araldite CY212. Sections were taken approximately 2 µm thick. Staining with 1% methylene blue was then performed. The slides were kept on a hot plate at 100–110 °C for approximately 40–45 s and then washed with tap water and rinsed. For descriptive analysis, the sections were first examined under a light microscope. Tissue blocks were cut to prepare ultrathin sections after region of interest identification. Ultrathin sections (60×90 nm) taken with a Leica EM UC7 ultramicrotome were stained with uranyl acetate and lead citrate. The stained sections were visualized and photographed on a Hitachi HT7800 120 kV transmission electron microscope (TEM).

Statistical analysis

In the descriptive statistical analysis, median scores with interquartile ranges (IQR) were used to summarize numerical variables, while frequencies and percentages were reported for categorical variables. Statistical analyses were conducted using two approaches. First, the thickness of the dura mater was evaluated using the Mann–Whitney *U* test. Second, a chi-square test was employed to assess dura mater fibrosis and arachnoid involvement. Statistical significance was established at $p<0.05$, with α set at 0.05 for Type I error. All analyses were performed using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY, USA).

Results

Table 1 presents the results of dura mater thickness measurements. Subjects in the tranexamic acid group exhibited significantly thinner dura mater compared to the control group ($p=0.001$). In the stained axial sections (Table 2), the control group predominantly displayed severe scarring, with Grade 3 fibrosis observed in eight of ten rats (80%). Only one rat exhibited Grade 2 fibrosis, and one (10%) showed Grade 1 fibrosis (Fig. 1). In contrast, the tranexamic acid group demonstrated markedly improved outcomes, with minimal scarring (Grade 1) in seven of ten rats (70%), moderate scarring (Grade 2) in two rats, and severe scarring (Grade 3) in only one rat (10%) (Fig. 2). Statistical analysis revealed a significant difference in fibrosis grades along the dura mater between the tranexamic acid and control groups ($p=0.006$). Additionally, tranexamic acid treatment resulted in significantly lower arachnoid involvement scores in the treatment group ($p=0.02$), as detailed in Table 3.

Table 2 Tranexamic Acid and the control groups scar tissue grades

	N	Grade 0	Grade 1	Grade 2	Grade 3
Control group	10	0	1 (10%)	1 (10%)	8 (80%)
Tranexamic acid group	10	0	7 (70%)	2 (20%)	1 (10%)

Significantly difference was found between tranexamic acid and the control groups groups, $p=0.006$

Electron microscopic evaluation of the control group revealed dense, organized bundles of collagen fibers, numerous scattered erythrocytes, and highly active fibroblasts with well-developed rough endoplasmic reticulum (Fig. 3). In contrast, the tranexamic acid group showed collagen fibers forming thinner, less organized bundles oriented in multiple directions, with significantly fewer

Table 3 Tranexamic Acid and the control groups arachnoid adhesion results

	N	Yes	No
Control group	10	8 (80%)	2 (20%)
Tranexamic acid group	10	1 (10%)	9 (90%)

Significantly difference was found between tranexamic acid and the control groups, $p = 0.02$

active fibroblasts and only occasional fibrocytes interspersed among them (Fig. 4).

Discussion

The craniectomy revisions may often result in extended surgical duration, increased blood loss, and potential damage to the dura mater and brain tissue. Excessive adhesive tissue formation makes this kind of surgery complex to perform [3]. Various biological and synthetic materials have been investigated to prevent scar formation [1, 24]. These include haemostatic sponges [15], biologically absorbed barrier gels [23], fat grafts [12], hyaluronic acid [30], carboxymethylcellulose gels [18], a combination of dextran sulfate and gelatine (Adcon-L, Gliatech), 5-fluorouracil, cyclosporine [41], and radiation therapy [2]. Despite these efforts, the outcomes of these investigations have shown only limited success, and their clinical application has not yet proven effective.

Complex cranial procedures involving both supra- and infratentorial compartments present significant surgical challenges, often complicated by adhesions and limited dissection fields. Techniques aimed at minimizing such adhesions—like the use of antifibrotic agents—may support surgical efficiency, as also discussed in rare dual-compartment hematoma drainage strategies [32]. Fibrotic adhesions are a common challenge not only in cranial surgeries but also in spinal procedures such as tethered cord syndrome, as previously described by Tabanli et al. [33].

Adhesion development is widely believed to involve the transformation of fibrinous adhesions into fibrous ones through fibrin deposition. Thus, one might assume that introducing fibrin to a surgical site could promote adhesion formation [11]. However, numerous studies on animals and humans using fibrin-based materials do not support this assumption [21, 38]. In the present study, we have investigated the possibility that fibrin may be an adhesion prevention agent due to its potential benefits. As the end product of the coagulation cascade, fibrin is formed when thrombin acts on fibrinogen, removing fibrinopeptides A and B to produce fibrin monomers that aggregate into a gel [12]. Fibrin can reduce adhesions by forming a barrier once fully polymerized, preventing attachment to other surfaces [34, 36].

Although it is thought that reducing scar tissue at the surgical site may impair dural healing and increase the risk of cerebrospinal fluid leakage, no conclusive evidence supports this claim [31]. Instead, numerous studies have identified key risk factors for CSF leakage, which can be categorized as either patient-related or surgery-related. Patient-specific risks include male sex, younger age, a high body mass index, and diabetes [7, 13]. On the surgical side, factors such as infratentorial procedures and prolonged operative time have been associated with an increased risk of CSF leakage [13, 28]. While there is no existing literature on the effect of tranexamic acid on cerebrospinal fluid leaks, Esposito et al. have suggested that fibrin sealants used in neurosurgery may help achieve a watertight dural closure. Their findings indicate that these sealants could be effective in preventing CSF leaks while maintaining an acceptable safety profile [10].

Tranexamic acid, a synthetic lysine analog, inhibits fibrinolysis by reversibly blocking plasminogen's lysine binding sites [20]. This medication has been widely utilized to prevent bleeding in various gynaecological procedures, including placental haemorrhage, postpartum blood loss, and cervical conization [40]. Additionally, tranexamic acid has demonstrated efficacy in reducing blood loss following oral surgery for haemophilia patients and has proven effective as an oral rinse for dental patients on anticoagulant therapy [26, 35]. The drug has also shown benefits in decreasing blood loss during orthotopic liver transplantation and transurethral prostate surgery [22, 25]. Moreover, it has been successful in lowering rebleeding rates in patients with traumatic hyphema [8]. When the literature is examined in detail, it shows that tranexamic acid was experimentally used in different anatomical sites in different specialties rather than as a blood preventing agent. Wiseman et al. investigated the relationship between different doses and amounts of antifibrinolytic agents, tranexamic acid, and aprotinin with the development of adhesions in abdominal wounds. Also, both tranexamic acid and aprotinin were shown to reduce the incidence and severity of adhesions [39]. In addition, Sahin et al. reported that tranexamic acid affects the bone formation process. They have shown that fibrinolysis suppression reduces the quality and stability of fusion without a delay in bone formation [29].

Circi et al. [5] found that local application of 30 mg of tranexamic acid at the laminectomy site and systematic use of 30 mg/kg of tranexamic acid reduced the formation of epidural fibrosis. However, they did not measure dura mater thickness in their study. The dura mater is the most affected meningeal layer during the formation of epidural adhesions. We evaluated both dura mater thickness and electron microscopic evaluation in our current

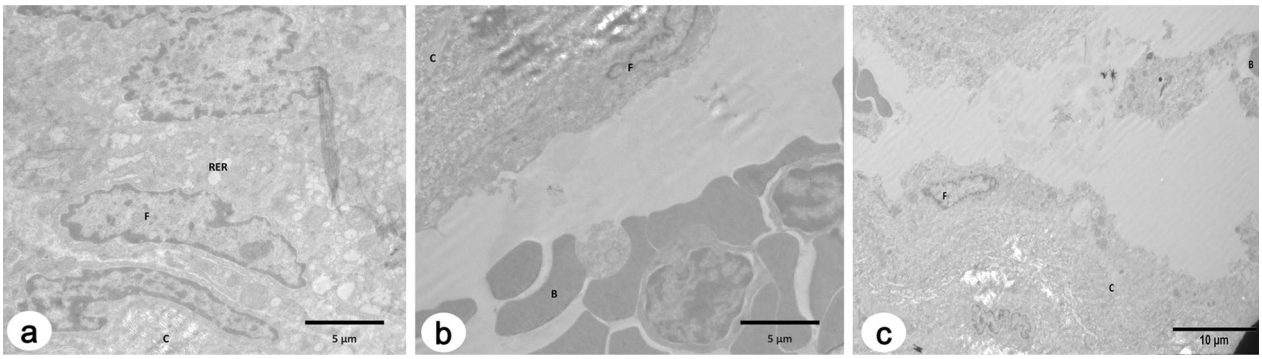

Fig. 3 Control group electron microscopy demonstrates. **A** Dural section with active fibroblast (F) with well-developed rough endoplasmic reticulum (RER) and collagen fibers (C). **B** Active fibroblast (F) with well oriented collagen bundles (C) are observed. In the opposite corner of the picture blood elements are seen (B). **C** Thick bundles of collagen bundles (C) overlaying active fibroblast (F) are observed. Some erythrocytes (R) are seen in the dural space

Fig. 4 Tranexamic acid group electron microscopy demonstrates: **A** Collagen fibers (C) in various directions and a fibrocyte (F) are observed. **B** Collagen fibers (C) extending in various directions and a less active fibroblast (F) is observed. **C** Collagen fibers (C) extending in various directions and a less active fibroblast (F) is observed

study. Electron microscopic evaluation provided us with much more data toward understanding the mechanism of action of the drug, since no previous evaluation has been performed on this subject. The analysis of dura mater thickness revealed a statistically significant variance between the tranexamic acid and the control groups ($p=0.001$). Similarly, the evaluation of fibrosis density [14] demonstrated a statistically significant difference when comparing the tranexamic acid-treated group to the control group ($p=0.006$). The dura mater thickness results were consistent with the fibrosis density assessments. No inflammatory reaction at the wound site was detected in any case, nor was there was any neuronal involvement. In addition to the pathological evaluation, electron microscopic examination showed that tranexamic acid prevents fibroblastic transformation of fibrocytes and inhibits collagen maturation preventing dural fibrosis.

Tranexamic acid is currently used widely as a haemostatic agent in various parts of the body, both systemically and locally, by medical departments worldwide. Numerous published studies have determined the safe dose range and frequency. The effect of tranexamic acid on bone healing and tendon healing has been investigated [9], but only one study has examined its effect on epidural fibrosis in a lumbar laminectomy model. This study has examined its systemic and local effects in a single dose range and has found it to be effective on epidural fibrosis [5]. Our research represents the first investigation in the scientific literature to assess the local application of tranexamic acid on the craniectomy site using a craniectomy model. This novel approach evaluates the efficacy of this treatment method in the context of cranial surgery. We have shown that tranexamic acid effectively prevents adhesion in the craniectomy region in a statistically significant manner and we have supported our results with electron microscopic findings. The advantages of less adhesions on 2nd stage surgeries include shorter operation times, reduced anaesthesia exposure, and lower associated risks [17]. Additionally, less blood loss decreases the need for transfusions and related complications [37].

With fewer adhesions, dissection is easier, reducing the risk of accidental dural tears and preventing cerebrospinal fluid leakage. This also protects underlying brain tissue from mechanical trauma during dissection, minimizing the risk of cortical haemorrhage and neurological deficits [27]. Less tissue manipulation and shorter procedure times further reduce infection risks. Moreover, more precise dissection allows for optimal bone flap positioning [4].

Several limitations should be acknowledged. First, the study was performed with small sample size. Second, since only a single dose of tranexamic acid was evaluated, the generalizability of the results may be constrained. Future studies should investigate varying doses to determine whether the observed effects are dose dependent. Third deficiency in our study is that tranexamic acid was not examined parenterally. Fourth, while Wistar rats were used in this study, which may not fully replicate human surgical conditions. Finally, incorporating additional biochemical analyses of inflammatory markers could strengthen the pathological assessment and provide a more comprehensive evaluation of postoperative efficacy.

Conclusion

This study shows that administering tranexamic acid after craniectomy significantly reduces epidural fibrosis and adhesion formation in rats—a key finding with direct implications for 2nd stage cranioplasty. Although this is an experimental study, the observed reduction in adhesions could substantially decrease operative time, blood loss, and complication risks in subsequent surgeries in humans. Notably, tranexamic acid provided these benefits without any observed adverse effects in rats, suggesting it could become a valuable tool in future neurosurgical practice.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s40001-025-02634-z.

Supplementary Material 1.

Supplementary Material 2.

Supplementary Material 3.

Author contributions

Ö.Ş. and T.T.: study conception and design, control/supervision, data collection and processing, surgical procedures, pharmacological applications, writing the article, final manuscript approval A.F, H.S.B and M.Ç.: data analysis or interpretation, literature review, prepared figures, critical manuscript revision.

Funding

No funding was received no financial support.

Availability of data and materials

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The study was conducted with the approval of Ankara Training and Research Hospital Animal Experiments and Local Ethics Committee decision with permission number 775.

Competing interests

The authors declare no competing interests.

Received: 9 January 2025 Accepted: 23 April 2025
Published online: 06 May 2025

References

1. Abitbol JJ, Lincoln TL, Lind BI, Amiel D, Akeson WH, Garfin SR. Preventing postlaminectomy adhesion A new experimental model. Spine. 1994;19(16):1809–14. https://doi.org/10.1097/00007632-199408150-00004.
2. Bora H, Aykol SV, Akyürek N, Akmansu M, Ataoglu O. Inhibition of epidural scar tissue formation after spinal surgery: external irradiation vs. spinal membrane application. Int J Radiat Oncol Biol Phys. 2001;51(2):507–13. https://doi.org/10.1016/s0360-3016(01)01647-9.
3. Cemil B, Tun K, Kaptanoglu E, Cevirgen B, Gurcay AG, Kaymaz F, Tekdemir I. The effect of mitomycin C as fibrosis preventive agent during craniectomies. Br J Neurosurg. 2009;23(3):304–8. https://doi.org/10.1080/02688690802603913.
4. Cho YJ, Kang SH. Review of cranioplasty after decompressive craniectomy. Korean J Neurotrauma. 2017;13(1):9–14. https://doi.org/10.13004/kjnt.2017.13.1.9.
5. Circi E, Atici Y, Baris A, Senel A, Leblebici C, Tekin SB, Ozturkmen Y. Is tranexamic acid an effective prevention in the formation of epidural fibrosis? Histological evaluation in the rats. J Korean Neurosurg Soc. 2023;66(5):503–10. https://doi.org/10.3340/jkns.2022.0249.
6. Colomina MJ, Contreras L, Guilabert P, Koo M, Ndez ME, Sabate A. Clinical use of tranexamic acid: evidences and controversies. Braz J Anesthesiol (Elsevier). 2022;72(6):795–812. https://doi.org/10.1016/j.bjane.2021.08.022.
7. Copeland WR, Mallory GW, Neff BA, Driscoll CL, Link MJ. Are there modifiable risk factors to prevent a cerebrospinal fluid leak following vestibular schwannoma surgery? J Neurosurg. 2015;122(2):312–6. https://doi.org/10.3171/2014.10.JNS14432.
8. CRASH-2 trial collaborators, Shakur H, Roberts I, Bautista R, Caballero J, Coats T, Dewan Y, El-Sayed H, Gogichaishvili T, Gupta S, Herrera J, Hunt B, Iribhogbe P, Izurieta M, Khamis H, Komolafe E, Marrero MA, Mejía-Mantilla J, Miranda J, Morales C, Yutthakasemsunt S. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. Lancet (London, England). 2010;376(9734):23–32. https://doi.org/10.1016/S0140-6736(10)60835-5.
9. Dunn CJ, Goa KL. Tranexamic acid: a review of its use in surgery and other indications. Drugs. 1999;57(6):1005–32. https://doi.org/10.2165/00003495-199957060-00017.
10. Esposito F, Angileri FF, Kruse P, Cavallo LM, Solari D, Esposito V, Tomasello F, Cappabianca P. Fibrin sealants in dura sealing: a systematic literature review. PLoS ONE. 2016;11(4): e0151533. https://doi.org/10.1371/journal.pone.0151533.
11. Gauwerky JF, Mann J, Bastert G. The effect of fibrin glue and peritoneal grafts in the prevention of intraperitoneal adhesions. Arch Gynecol Obstet. 1990;247(4):161–6. https://doi.org/10.1007/BF02389540.
12. Gill GG, Scheck M, Kelley ET, Rodrigo JJ. Pedicle fat grafts for the prevention of scar in low-back surgery. A preliminary report on the first 92 cases. Spine. 1985;10(7):662–7. https://doi.org/10.1097/00007632-198509000-00012.

13. Ha BJ, Cheong JH, Yi HJ. Risk factors for cerebrospinal fluid leakage after craniotomy and the efficacy of dural sealants application versus dural suturing alone. Nerve. 2016;2(2):22–5.
14. He Y, Revel M, Loty B. A quantitative model of post-laminectomy scar formation. Effects of a nonsteroidal anti-inflammatory drug. Spine. 1995;20(5):557–80. https://doi.org/10.1097/00007632-199503010-00010.
15. Jacobs RR, McClain O, Neff J. Control of postlaminectomy scar formation: an experimental and clinical study. Spine. 1980;5(3):223–9. https://doi.org/10.1097/00007632-198005000-00004.
16. Kawaguchi T, Hosoda K, Shibata Y, Koyama J. Expanded polytetrafluoroethylene membrane for prevention of adhesions in patients undergoing external decompression and subsequent cranioplasty. Neurol Med Chir. 2003;43(6):320–4. https://doi.org/10.2176/nmc.43.320.
17. Kim YH, Lee CH, Kim CH, Son DW, Lee SW, Song GS, Sung SK. Clinical efficacy and safety of silicone elastomer sheet during decompressive craniectomy: anti-adhesive role in cranioplasty. Brain Sci. 2021;11(1):124. https://doi.org/10.3390/brainsci11010124.
18. Kitano T, Zerwekh JE, Edwards ML, Usui Y, Allen MD. Viscous carboxymethylcellulose in the prevention of epidural scar formation. Spine. 1991;16(7):820–3. https://doi.org/10.1097/00007632-199107000-00023.
19. Kurt G, Aytar MH, Doğulu F, Cemil B, Erdem O, Baykaner MK, Ceviker N. A comparison of the local effectiveness of mitomycin C, aprotinin, and Adcon-L in experimental peridural fibrosis. Surg Neurol. 2008;70(6):608–13. https://doi.org/10.1016/j.surneu.2007.07.071.
20. Levy JH, Dutton RP, Hemphill JC 3rd, Shander A, Cooper D, Paidas MJ, Kessler CM, Holcomb JB, Lawson JH, Participants HS. Multidisciplinary approach to the challenge of hemostasis. Anesth Analg. 2010;110(2):354–64. https://doi.org/10.1213/ANE.0b013e3181c84ba5.
21. Lindenberg S, Steentoft P, Sørensen SS, Olesen HP. Studies on prevention of intra-abdominal adhesion formation by fibrin sealant. An experimental study in rats. Acta Chirurgica Scand. 1985;151(6):525–7.
22. Lloyd TD, Neal-Smith G, Fennelly J, Claireaux H, Bretherton C, Carr AJ, Murphy M, Kendrick BJ, Palmer AJR, collaborators,. Peri-operative administration of tranexamic acid in lower limb arthroplasty: a multicentre, prospective cohort study. Anaesthesia. 2020;75(8):1050–8. https://doi.org/10.1111/anae.15056.
23. Lo H, Frederickson RC. Use of ADCON in neurosurgery: preclinical review. Neurol Res. 1999;21(Suppl 1):S27–32. https://doi.org/10.1080/01616412.1999.11741023.
24. MacMillan M, Stauffer ES. The effect of omental pedicle graft transfer on spinal microcirculation and laminectomy membrane formation. Spine. 1991;16(2):176–80. https://doi.org/10.1097/00007632-199102000-00014.
25. Mina SH, Garcia-Perdomo HA. Effectiveness of tranexamic acid for decreasing bleeding in prostate surgery: a systematic review and meta-analysis. Central Eur J Urol. 2018;71(1):72–7. https://doi.org/10.5173/ceju.2017.1581.
26. Monaco F, Nardelli P, Pasin L, Barucco G, Mattioli C, Di Tomasso N, Dalessandro G, Giardina G, Landoni G, Chiesa R, Zangrillo A. Tranexamic acid in open aortic aneurysm surgery: a randomised clinical trial. Br J Anaesth. 2020;124(1):35–43. https://doi.org/10.1016/j.bja.2019.08.028.
27. Preul MC, Campbell PK, Garlick DS, Spetzler RF. Application of a new hydrogel dural sealant that reduces epidural adhesion formation: evaluation in a large animal laminectomy model. J Neurosurg Spine. 2010;12(4):381–90. https://doi.org/10.3171/2009.10.SPINE09537.
28. Russel A, Hoffmann CP, Nguyen DT, Beurton R, Parietti-Winkler C. Can the risks of cerebrospinal fluid leak after vestibular schwannoma surgery be predicted? Otol Neurotol. 2017;38(2):248–52. https://doi.org/10.1097/MAO.0000000000001267.
29. Sahin E, Berk H, Ozkal S, Keskinoglu P, Balci P, Balci A. Effect of local tranexamic acid on the quality of bone healing in a rat spinal fusion model. Spine Surg Related Res. 2021;6(2):151–8. https://doi.org/10.22603/ssrr.2021-0113.
30. Songer MN, Ghosh L, Spencer DL. Effects of sodium hyaluronate on peridural fibrosis after lumbar laminotomy and discectomy. Spine. 1990;15(6):550–4. https://doi.org/10.1097/00007632-199006000-00022.
31. Spinks RL, Baker SN, Jackson A, Khaw PT, Lemon RN. Problem of dural scarring in recording from awake, behaving monkeys: a solution using 5-fluorouracil. J Neurophysiol. 2003;90(2):1324–32. https://doi.org/10.1152/jn.00169.2003.
32. Tabanli A, Yilmaz H. Surgical technique for draining a concomitant supra- and infratentorial epidural hematomas. Turk Neurosurg. 2024;34(4):618–23. https://doi.org/10.5137/1019-5149.JTN.43250-22.4.
33. Tabanli A, Akcay E, Yilmaz H, Ozdemir S, Mete M, Selcuki M. Surgical outcomes of tethered cord syndrome in patients with normal conus medullaris and filum terminale without urologic symptoms. Child's Nerv Syst. 2024;41(1):47. https://doi.org/10.1007/s00381-024-06713-0.
34. Takeuchi H, Awaji M, Hashimoto M, Nakano Y, Mitsuhashi N, Kuwabara Y. Reduction of adhesions with fibrin glue after laparoscopic excision of large ovarian endometriomas. J Am Assoc Gynecol Laparosc. 1996;3(4):575–9. https://doi.org/10.1016/s1074-3804(96)80033-8.
35. Tengborn L, Blombäck M, Berntorp E. Tranexamic acid–an old drug still going strong and making a revival. Thromb Res. 2015;135(2):231–42. https://doi.org/10.1016/j.thromres.2014.11.012.
36. Tulandi T. Effects of fibrin sealant on tubal anastomosis and adhesion formation. Fertil Steril. 1991;56(1):136–8. https://doi.org/10.1016/s0015-0282(16)54432-x.
37. Vakis A, Koutentakis D, Karabetsos D, Kalostos G. Use of polytetrafluoroethylene dural substitute as adhesion preventive material during craniectomies. Clin Neurol Neurosurg. 2006;108(8):798–802. https://doi.org/10.1016/j.clineuro.2005.11.026.
38. Wiseman DM, Kamp L, Linsky CB, Jochen RF, Pang RH, Scholz PM. Fibrinolytic drugs prevent pericardial adhesions in the rabbit. J Surg Res. 1992;53(4):362–8. https://doi.org/10.1016/0022-4804(92)90062-5.
39. Wiseman D, Lyachovetsky Y, Keidan I, Trout JR, Nur I. The effect of tranexamic acid in fibrin sealant on adhesion formation in the rat. J Biomed Mater Res Part B Appl Biomater. 2004;68(2):222–30. https://doi.org/10.1002/jbm.b.20016.
40. WOMAN Trial Collaborators. Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial. Lancet (London, England). 2017;389(10084):2105–16. https://doi.org/10.1016/S0140-6736(17)30638-4.
41. Yildiz KH, Gezen F, Is M, Cukur S, Dosoglu M. Mitomycin C, 5-fluorouracil, and cyclosporin A prevent epidural fibrosis in an experimental laminectomy model. Eur Spine J. 2007;16(9):1525–30. https://doi.org/10.1007/s00586-007-0344-8.

Publisher's Note