Clinical Neurology and Neurosurgery 176 (2019) 133–137

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Hemopatch® as a new dural sealant: A clinical observation☆

Stephan Nowak[a,*], Henry W.S. Schroeder[b], Steffen Fleck[b]

[a] Universitätsmedizin Greifswald, Klinik und Poliklinik für Neurochirurgie, Sauerbruchstraße, 17475, Greifswald, Germany
[b] Department of Neurosurgery, United States

ARTICLE INFO

Keywords:
Hemopatch®
Dural sealant
Dural closure
Csf fistula

ABSTRACT

Objectives: We analyzed our results using Hemopatch® as a new dural sealant after durotomy in cranial and spinal neurosurgical procedures.

Patients and methods: In our prospective single center study, we analyzed all patients who received Hemopatch® used as a dural sealant between October 2016 and May 2017. 34 patients received Hemopatch® used as a dural sealant in the study period. We included 23 (67.6%) female and 11 (32.3%) male patients. The mean age was 56 years (4–83 years). We included emergency and elective surgical procedures as well as spinal and cranial intradural surgery. We did not exclude any type of underlying pathology. We took note of the general patient data, the size of Hemopatch® used, the type of dural closure, and the postoperative stay. Additionally, we recorded the type of dural closure (watertight/ watertight with additional muscle patch/ not watertight with small or large defect (> 1 cm) remaining) and of preoperative hydrocephalus as well as intraoperative ventricular opening.

Results: Hemopatch® was used in addition to the following dural closures: 11 (32.4%) watertight suture, 23 (67.6%) non-watertight suture. Three (8.8%) surgeries were emergency procedures. The site of surgery was as follows: 18 (52.9%) supratentorial, 16 (47.1%) infratentorial. A ventricular opening was performed in 13 (38.2%) cases. A hydrocephalus was present in 2 (5.9%) cases.

A revision surgery after use of Hemopatch® was performed in 2 (5.9%) patients. Postoperative CSF fistulas and infections were observed in 2 patients each.

Conclusion: We could demonstrate the safety and efficiency of Hemopatch® used as dural sealant after durotomy in microneurosurgical procedures. To confirm our promising results a larger prospective randomized controlled trial will be needed.

1. Introduction

After performing intradural cranial or spinal procedures a watertight dural closure should be achieved to reduce the risk of cerebrospinal fluid (CSF) leakage. Several studies could demonstrate that a CSF leakage increases the morbidity, prolongs the hospital stay, and may lead to revision surgery [6]. That means that not only the perioperative risks increase for the individual patient, but also the costs [3].

Therefore, many techniques and sealant agents have been developed to achieve a watertight dural closure [11]. One of the most often used sealing agents is a fibrinogen–thrombin-coated collagen pad. Its successful use as a hemostat but also as a dural sealant could be demonstrated [7]. Nonetheless, after established use of fibrinogen–thrombin-coated collagen pads prospective randomized controlled studies could demonstrate no further reduction of CSF leakage compared to traditional running suture alone [5]. Many new sealing agents have been used in the neurosurgical practice with similar results in spinal and cranial surgery [13]. Compared to traditional absorbable fibrin sealant patches the economic costs for those are quite high and therefore not a common alternative.

One of the newer hemostatic and sealing agents is Hemopatch® (Baxter Deutschland GmbH; Germany). The Hemopatch® is a pad with a self-adhering surface and sheet-like backing. This collagen patch uses a new self-adhering surface at its active side. The active agent is a rapid protein-reactive monomer which binds to tissue through covalent amide bonds between Polyethylenglycol (PEG) and tissue proteins and

Abbreviations: CSF, cerebrospinal fluid; NHS-PEG, succinimidyl carboxyl methyl ester; PDS, polydioxanon; PEG, polyethylenglycol; SAH, subarachnoid hemorrhage

☆ I, Dr. Nowak, certify that this manuscript is a unique submission and is not being considered for publication, in part or in full, with any other source in any medium. The senior author attended one workshop as introduction to Hemopatch®. Figure one was provided in courtesy of Baxter USA. There is no disclosure of funding to report for any author.

* Corresponding author.
E-mail address: stephan.nowak@uni-greifswald.de (S. Nowak).

https://doi.org/10.1016/j.clineuro.2018.12.009
Received 5 November 2018; Received in revised form 7 December 2018; Accepted 10 December 2018
Available online 11 December 2018
0303-8467/

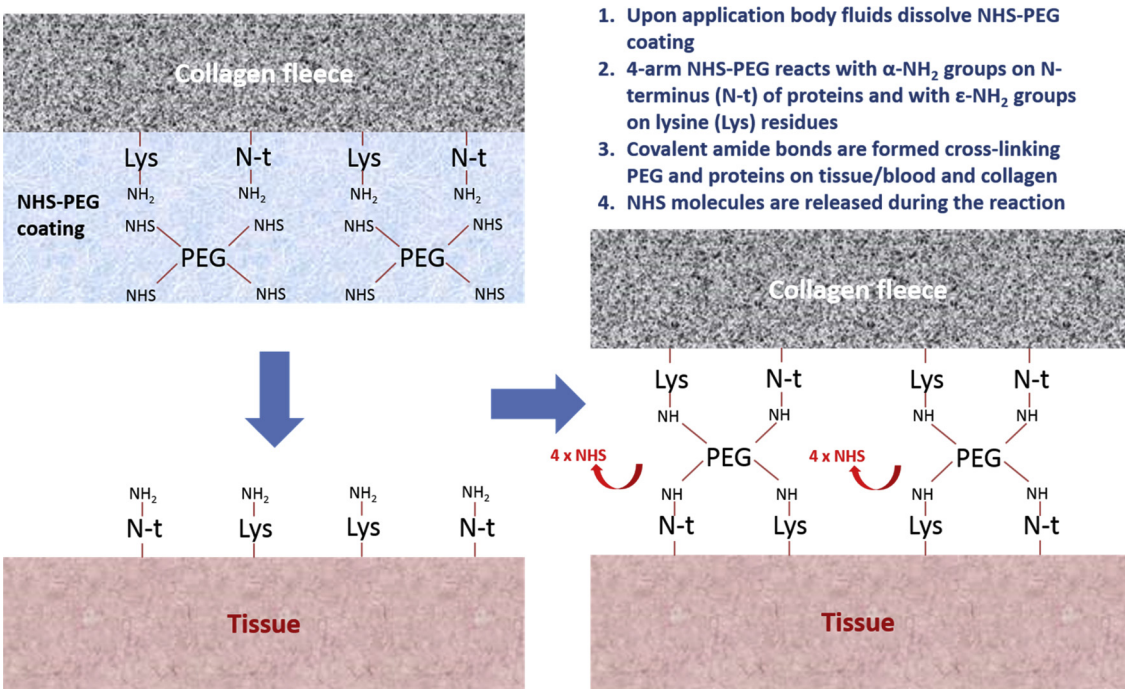

Fig. 1. A chemical Model of rapid protein-reactive monomer binding to tissue through covalent amide bonds between Polyethylenglycol (PEG) and tissue proteins and collagen; provided by courtesy of Baxter USA.

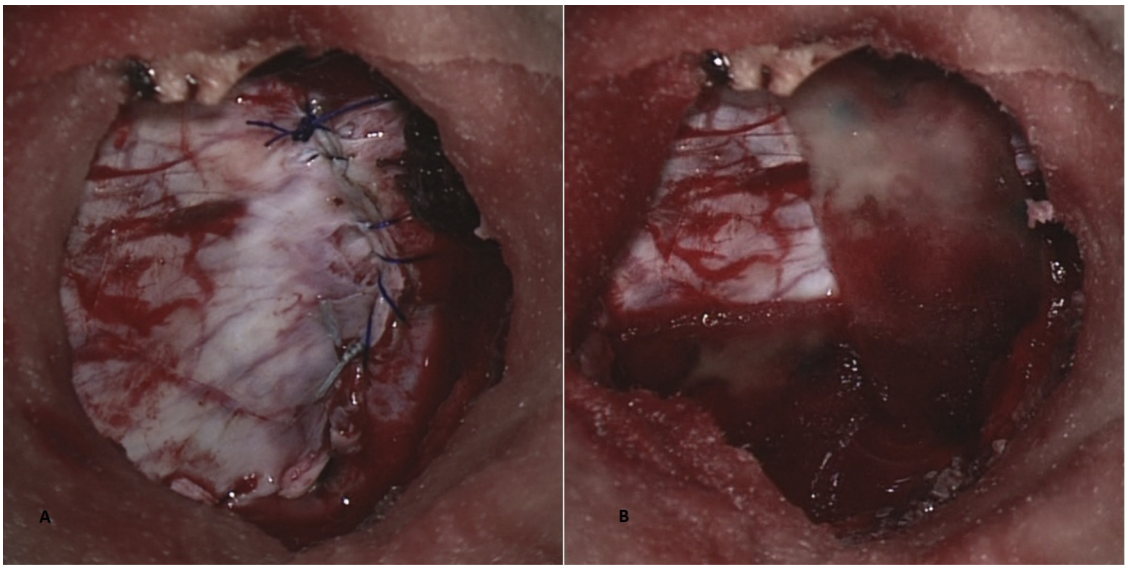

Fig. 2. Intraoperative application of Hemopatch as dural sealant after retrosigmoidal approach. A: watertight dural closure. B: applied Hemopatch.

collagen [9]. Fig. 1 shows a biochemical model. Hemopatch® could demonstrate its more effective use as hemostatic agent and sealant in comparison to fibrinogen-thrombin-coated collagen pads. Especially due to its dual mechanism of action which uses a porous collagen matrix to promote greater hemostatic effects and the protein-binding layer meaning a greater adhesiveness to the side of action [9]. This makes the Hemopatch® also an excellent alternative to classic fibrinogen-thrombin-coated collagen pads as a dural sealant. Fig. 2 shows an intraoperative application of Hemopatch® as dural sealant after retrosigmoid craniotomy. In this study, we analyzed our experience with the new dural sealant "Hemopatch®".

2. Material and methods

2.1. Participants

In our prospective single center study, we analyzed 37 patients who received Hemopatch® used as a dural sealant between October 2016 and May 2017. The inclusion criteria contain all cases who underwent craniotomy were Hemopatch® was used as dural sealant after durotomy at any side. For a general overview of the effectiveness of Hemopatch® in the broad clinical setting, we included emergency and elective surgical cranial intradural procedures. We did not exclude any type of underlying pathology the patient was operated on. We excluded 1 transnasal, transsphenoidal and 2 spinal procedures. As the numbers are too low to make a statistical impact. Always, the surgeon decided on

his own clinical experience, in every single case independently, to use or not to use Hemopatch® to achieve a watertight dural closure. In our clinical department a collagen sealing agent will be used when a watertight suture cannot be achieved by running suture alone. Small to medium sized defects will usually be closed with the use of a muscle patch. Large defects will be closed by either periost or pericard (XenoSure LeMaitre Vascular GmbH; Germany) grafting together with a collagen sealant overlay.

The dural suture was accomplished using Prolene 4-0 (Johnson & Johnson Medical GmbH; Germany).

2.2. Data collection

We obtained the general patient data, the size of Hemopatch® used, the type of dural closure and the postoperative stay. Special note we took on the type of dural closure (watertight/ watertight with additional muscle patch/ not watertight with small or large defect remaining). Furthermore, we recorded pre-and postoperative hydrocephalus and intra-operative ventricular opening.

To define the efficacy of Hemopatch as dural sealant we took special note of how the primary dural closure, before the application of Hemopatch, was accomplished and whether a dural defect remained as potential source of dural fistula. Special risk factors favoring a dural fistula (intra-operative ventricular opening, the use of a subgaleal drainage and hydrocephalus) were noted. Also, any sign of dural fistula (subgaleal CSF accumulation or open fistula as well as rhinoliquorrhoe) in the postoperative course was clinically evaluated and documented.

For safety analyses any sign of surgical site infection was clinically evaluated every day. Blood analysis for infect parameters (CRP and leucocyte count) was performed at the first postoperative day and when clinical signs of infection (high temperature, profound night sweating and cardiopulmonary signs) were reported. We analyzed the surgical report for detailed information.

The data analysis was done by using Microsoft Excel and statistical percental comparison. To calculate the p value we used Chi-square score with a significance level of 0.05.

2.3. Statistical analysis

We included 23 (67.6%) female and 11 (32.3%) male patients. The mean age at time of surgery was 56 years (4–83 years). All procedures performed were with dural opening. Three (8.8%) patients were emergency procedures. They included a subarachnoid hemorrhage due to a ruptured middle cerebral artery (MCA) aneurysm, an acute subdural hematoma, and an intracerebellar bleeding. In 18 (52.9%) patients a supratentorial craniotomy and in 16 patients (47.1%) an infratentorial craniotomy was performed. Surgery was performed due to meningiomas in 6 (17.6%) patients, due to glioma and other tumor-like lesions (pineal cysts, arachnoid cysts, metastasis etc.) in 18 (53%) patients. Other etiologies included bleeding, facial spasm, aneurysm etc. in 10 (29.4%) patients. A ventricular opening occurred in 13 (38.2%) patients. A hydrocephalus was present in 2 (5.9%) patients: in one patient due to an intracerebellar bleeding with intraventricular hemorrhage and in the other patient due to multiple revisions by recurring grade 3 glioma.

The size of Hemopatch® is divided in small (2.7 × 2.7 cm), medium (4.5 × 4.5 cm) and large (4.5 × 9.0 cm). The small size was used in 7 (20.6%) patients, the medium size in 17 (50%) patients, and the large size in the remaining 10 (29.4%) patients.

The study was approved by the ethical commission board of the university medicine Greifswald.

3. Results

To support a nearly watertight suture Hemopatch® was used in 12 (35.3%) patients. In most of the patients (64.7%), a watertight suture could not be achieved by running suture alone. In 10 (29.4%) patients, a watertight suture was achieved by muscle-patch with an overlying Hemopatch®. In 6 (17.7%) patients, the dura had to be closed by using periost or pericard (XenoSure LeMaitre Vascular GmbH; Germany). In 5 (14.7%) patients, a small defect remained after dural suture which was sealed by Hemopatch® alone. In 1 (2.9%) patient a frontal key-hole approach with a dural defect of 1 cm was sealed by using Hemopatch® alone.

We identified 9 (26.5%) patients, who received a subgaleal drainage before wound closure. A ventricular opening occurred in 13 (38.2%) patients. A hydrocephalus was present in 2 (5.9%) patients: in one patient due to an intracerebellar bleeding with intraventricular hemorrhage and in the other patient due to multiple revisions by recurring grade 3 glioma. A postoperative external ventricular drainage was placed in 2 (5.9%) patients. In 1 patient, due to cerebellar hemorrhage as primary surgery indication and in 1 patient due to SAH after ruptured MCA aneurysm.

In the postoperative course a lumbar drainage was used in 2 (5.9%) patients. One was used perioperatively in giant meningeoma surgery. One was used due to CSF fistula for three days. A postoperative CSF fistula was present in 2 (5.9%) patients ($p = 0.29$). Only in 1 (2.9%) of these patients a surgical revision was needed. This was after a retrosigmoid approach for microvascular decompression of hemifacial spasm and postoperative rhinoliquorrhea necessitating revision surgery. The primary dural repair was achieved by muscle patch, fibrin glue, and small sized Hemopatch®. In the other patient, a subgaleal CSF accumulation could be treated by lumbar drainage for three days. In the latter case, the primary dural repair after sphenoidal meningioma surgery was achieved by running suture and muscle patch with overlaying large Hemopatch®. In both cases, no subgaleal drainage was used.

A postoperative infection was present in 2 (5.9%) patients. In 1 patient, a surgical revision was needed due to an epidural abscess after acute subdural hematoma evacuation. In the other patient, the laboratory analysis of the CSF could not rule out infection. An antibiotic therapy was started for 9 days despite of no clinical signs of infection (no meningism, no fever).

A revision surgery was performed in 2 (5.9%) patients. In 1 patient due to a wound infection and in 1 patient a decompressive hemicraniectomy was performed due to brain edema after giant meningioma surgery.

Not included in our statistical analysis were two spinal cases and one endoscopic transnasal transsphenoidal surgery:

In our two spinal cases primary watertight suture after lumbar hemilaminotomy and intradural tumor resection could be achieved and a small Hemopatch was used to support the suture. In both cases the mobilization was started at the first post-operative day. No signs attributed to low CSF pressure (headache, dizziness) were seen in the post-operative stay.

Also, we used Hemopatch once to seal the diaphragm sellae after endoscopic transnasal transsphenoidal hypophyseal adenoma resection. The sella floor was reconstructed and sealed with Polydioxanon (PDS) foil and gelantin sponge (Gelaspon) (Bausch + Lomb; Germany). The post-operative stay was uneventful. No rhinoliquorrhoe or meningitis occurred.

4. Discussion

We could demonstrate in our study that Hemopatch® can safely be used as a dural sealant in cranial procedures. With a new active agent at its self-adhering site Hemopatch® can easily be used also in cases were a watertight dural suture cannot be achieved otherwise [9]. In our series, a post-operative csf fistula occurred in 5.9% even though a watertight suture could not be achieved in 64.7% of cases and a ventricular opening occurred during surgery in 38.2% of cases. Due to our low cohort number we performed a Chi-square analysis. Our p Value is with 0.29 not significant. We could achieve comparable results. Therefore, in

comparison to other sealant agents, Hemopatch® can be a good alternative. Reviewing the literature, a conclusive solution which agent for dural closure should be used cannot easily be found. Even the question of necessity remains. Hutter et al., for example, could not show a statistically significant risk reduction of postoperative CSF leakage by using TachoSil® compared to a control-group in their prospective randomized study [5]. In other studies, a CSF leak occurred in up to 10.7% by using different sealant agents [8]. Also, when using different techniques like a sandwich technique for retrosigmoidal dural closure a csf leakage occurred in 8.6% in some studies [1]. In our department though, we feel that even if a tight dural repair can be achieved by suture alone (Prolene 4-0) small defects always remain, where the needle perforated the dura. This can be seen by performing a Valsalva maneuver after dural closure. Furthermore, an ongoing dural shrinkage due to scarring can be expected after every durotomy. In experimental models, it could be demonstrated that by using smaller needles and Gore-Tex suture, a watertight dural closures withstanding higher peak pressure levels could be achieved [2]. Therefore, we think the addition of an extra dural patch to support the running suture should always be considered were an absolute watertight suture cannot be achieved. Comparing our results with other agents we will find similar results for TachoSil®. Depending on the study performed, the results will vary between 1% and 4% of CSF leak occurrence [7,12]. But these results must be interpreted carefully as they are either retrospective in design and are not compared to a control group. However, none of these studies mention intraoperative ventricular opening and hydrocephalus as risk factors. In our series in 38.2% of the cases this occurred. This greatly elevates the risk of post-operative CSF-fistula and therefore emphasis our results in comparison. The best results could be achieved with the use of BioGlue (CryoLife Inc.; USA). A study performed by Kumar et al. could demonstrate an incidence of CSF fistula by only 0.93% [8]. What prevents the regular use of BioGlue is the premium price league and stands therefore not in comparison with Hemopatch® or TachoSil®.

The rate of infection is with 5.9% in the same range as other studies using TachoSil® as dural sealant [7]. Considering the general surgical site infection rate in cranial neurosurgical procedures with around 6%, using Hemopatch® does not elevate the incidence of post-operative infection [10]. Furthermore, the risk factors are importantly lower by using Hemopatch® compared to other collagen-based sealants especially TachoSil® as Hemopatch® does not use human blood components. Instead of, Succinimidyl Carboxyl Methyl ester (NHS-PEG) combined with the collagen matrix is responsible for the sealant mechanism as described above. Human blood components have a minimal risk of the transmission of blood transmitted diseases. Despite the newest technical standards and precautions used by the manufacturers the possibility of nonenveloped viruses or prions being transmitted still remains [14]. For secondary patient safety in case of pregnancy, transplanted and immunocompromised patients leaving Hemopatch® as the only alternative collagen-based sealant.

As one of the main components of Hemopatch® is nonhuman bovine collagen, the possibility of immunologic reactions exists. Up to date there are no reported cases of collagen sealant induced allergic reactions. This is in part due to the low immunogenicity of nonhuman bovine or equine collagen being used [4,15].

To summarize, the risk of csf leakage after durotomy is despite the use of modern sealing agents and different technical notes with 8–11% still high [7,8,12]. We could prove in a first prospective open application observation good and comparable results using Hemopatch as dural sealant with a csf fistula rate of 5,9% achieved in a group of cases with 647% of non-watertight dural suture and 382% of intra-operative ventricular opening.

The limitation of our study is the observational prospective design and the small cohort of only 34 patients. Furthermore, we included a broad spectrum of cranial approaches with different underlying diseases and emergency procedures which can lead to a bias.

5. Conclusion

Our study is the first clinical observation of the intraoperative application of Hemopatch® as a new dural sealant. We could demonstrate the safety and efficiency of Hemopatch® used as dural sealant even in cases were direct dural repair was not possible. To confirm our promising results of Hemopatch® as an alternative to other collagen-based sealants in the field of neurosurgery as dural sealant a prospective randomized controlled trial will be needed.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional committee (Ethikkommission an der Universitätsmedizin Greifswald) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The registration number: BB 1,1,8117.

Informed consent

For this type of observational prospective study formal consent is not required. The patients received in every single case the standard therapy in regard to neurosurgical guidelines. No additional procedures were administered. Hemopatch is classified under the medicinal products act.

Conflict of interest

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript. The senior author attended one workshop as introduction to Hemopatch®.

Funding

No funding was received for this research.

References

[1] F. Arlt, C. Trantakis, W. Krupp, C. Renner, D. Winkler, G. Strauss, J. Meixensberger, Cerebrospinal fluid leak after microsurgical surgery in vestibular schwannomas via retrosigmoidal craniotomy, Neurol Res. 33 (9) (2009) 947–952.
[2] G.M. Ghobrial, C.M. Maulucci, M.J. Viereck, S. Beygi, A. Chitale, S. Prasad, et al., Suture choice in Lumbar Dural closure contributes to variation in leak pressures: experimental model, Clin. Spine Surg. 30 (6) (2017) 272–275.
[3] J.A. Grotenhuis, Costs of postoperative cerebrospinal fluid leakage: 1-year, retrospective analysis of 412 consecutive nontrauma cases, Surg Neurol. 64 (2005) 490–494.
[4] B. Horowitz, M. Busch, Estimating the pathogen safety of manufactured human plasma products: application to fibrin sealants and to thrombin, Transfusion 48 (2008) 1739–1753.
[5] G. Hutter, S. von Felten, M.H. Sailer, M. Schulz, L. Mariani, Risk factors for postoperative CSF leakage after elective craniotomy and the efficacy of fleece-bound tissue sealing against dural suturing alone: a randomized controlled trial, J. Neurosurg. 121 (3) (2014) 735–744.
[6] K.D. Kim, N.M. Wright, Polyethylene glycol hydrogel spinal sealant (DuraSeal spinal sealant) as an adjunct to sutured dural repair in the spine: results of a prospective, multicenter, randomized controlled study, Spine (Phila Pa 1976) 36 (2011) 1906–1912.
[7] J. Kivelev, F. Göhre, M. Niemelä, J. Hernesniemi, Experiences with Tachosil in microneurosurgery acta neurochir, Acta Neurochir. (Wien) 157 (2015) 1353–1357.
[8] A. Kumar, N.F. Maartens, A.H. Kaye, Evaluation of the use of BioGlue in neurosurgical procedures, J. Clin. Neurosci. 10 (2003) 661–664.
[9] K.M. Lewis, C.E. Kuntze, H. Gulle, Control of bleeding in surgical procedures: critical appraisal of HEMOPATCH (sealing hemostat), Med Devices (Auckl). 9 (2015) 1–10.
[10] A.N. Mallela, K.G. Abdullah, C. Brandon, A.G. Richardson, T.H. Lucas, Topical

vancomycin reduces surgical-site infections after craniotomy. A prospective, controlled study, Neurosurgery (2015), https://doi.org/10.1093/neuros/nyx559 [Epub ahead of print].
[11] P.A. Ozisik, S. Inci, F. Soylemezoglu, H. Orhan, T. Ozgen, Comparative dural closure techniques: a safety study in rats, Surg. Neurol. 65 (1) (2006) 42–47.
[12] M. Reddy, A. Schoggl, B. Reddy, W. Saringer, G. Weigel, C. Matula, A clinical study of a fibrinogen-based collagen fleece for dural repair in neurosurgery, Acta Neurochir. (Wien) 144 (2002) 265–269 discussion 269.
[13] J.T. Robertson, J. Soble-Smith, N. Powers, P.A. Nelson, Prevention of cerebrospinal fistulae and reduction of epidural scar with new surgical hemostat device in a porcine laminectomy model, Spine (Phila Pa 1976) 28 (19) (2003) 2298–2303.
[14] A. Toro, M. Mannino, G. Reale, I. Di Carlo, TachoSil use in abdominal surgery: a review, J Blood Med. 2 (2011) 31–36.
[15] L. Zhang, X. Niu, L. Sun, Z. She, R. Tan, W. Wang, Immune response of bovine sourced cross-linked collagen sponge for hemostasis, J. Biomater. Appl. 1 (2017) 885328217744080, , https://doi.org/10.1177/0885328217744080 [Epub ahead of print].