ORIGINAL ARTICLE

Intraoperative sealing of dura mater defects with a novel, synthetic, self-adhesive patch: application experience in 25 patients

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Abstract

Background. The quest for an ideal sealant for dura mater defects persists. The clinical experience with a novel, synthetic self-adhesive patch (TissuePatchDural®, Tissuemed, Leeds, UK) and its ability to prevent postoperative cerebrospinal fluid (CSF) leakage is described in this article. Methods. A recently developed, synthetic, self-adhesive patch was implanted in 25 patients who underwent intradural neurosurgical procedures. The indication for use was to adjunctively seal dura mater defects. The device is a multi-laminate consisting of thin films of a commonly used structural polymer, poly(lactide-co-glycolide) and a tissue reactive polymer providing fast and strong chemical bonding of the patch with the underlying biological surface. Intraoperative handling and efficacy, biocompatibility, and postoperative observations/ follow-up were analysed. Infectious complications, surgical wound features, and postoperative MRI scans were especially reviewed. The mean follow up period was 4.4 months. Results. The device provided fast and efficacious sealing of circumscribed dura mater defects within 1 minute in 23 patients (92%). Two of 25 patients developed a postoperative CSF leakage (8%), which may be secondary to particular factors predisposing these patients to CSF leaks. Surgical handling was straightforward. No infectious complications were recorded; furthermore, wound healing was unremarkable. No clinical evidence of foreign body reactions was observed. In 18 patients, postoperative MRI scans were available which did not show irregularities in any case. Conclusions. Safe and effective sealing can be accomplished with this bioabsorbable, purely synthetic and thin dural sealant, avoiding the application of foreign biologic material. The product has been shown to be effective in achieving watertight closure of the dura mater and has prevented CSF leakage in 92% of patients treated.

Keywords: CSF fistula; dura mater sealant; watertight dura closure.

Introduction

Watertight closure of the dura mater is a crucial step in neurosurgery as it prevents postoperative leakage of cerebrospinal fluid (CSF) and possible ingress of infectious agents causing an increased risk of postoperative meningitis.¹ Dura mater defects arising from tumours, trauma or friable dura conditions in recurrent operations sometimes lead to impossible primary dura closure. There is a significant demand for adjunctive materials to seal dura mater defects.

The ideal sealant is considered to be synthetic to avoid potential infection, should provide an instant and sustaining watertight closure of defects, and should be replaced by patient's own tissue with time. The range of surgical sealants and adhesives has included fibrinogen based liquid sealants, such as Tisseel, Beriplast, Bolheal and autologous preparations.²⁻⁴ Synthetic devices like polyethylene glycol (PEG) (DuraSeal®) or BioGlue® have been used as sealant to the repair dural defects following suared closure.⁴⁻⁵ The literature provides a number of reports in which sealants are used to prevent CSF loss following the insertion of a variety of dural substitutes, both synthetic⁶⁻¹⁰ and biological¹¹⁻¹⁵ in origin.

This report deals with TissuePatchDural®, a new synthetic device providing sealing properties in a patch form as opposed to a liquid. We evaluated the application of TissuePatchDural® in 25 patients, who underwent intradural neurosurgery and exhibited CSF effusion after dural suturing due to circumscribed defects. This paper is the first detailed description of the application of this newly designed dural sealant in neurosurgery in a larger patient cohort. A recent report has already suggested possible successful application in neurosurgery.¹⁶

Patients and methods

Material

TissuePatchDural® is a flexible, multilayered device comprising alternate layers of poly lactide-co-glycolide and poly N-vinyl-pyrrolidone-co-acrylic acid, co-N-hydroxysuccinimide ester of acrylic acid, 'Tissuebond'. Tissuebond

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itself is a bioadhesive material. As such it provides adhesion to the underlying dural margins, and it does not have to be sutured in. The patch is ready to use in contrast to the fibrinogen and PEG based products. Its transparency enables the surgeon to identify the underlying structures after usage, which is a useful feature especially in neurosurgical operations. The tissue response to the material leads to mild fibrosis surrounding the patch. The maximum thickness even after swelling is ≈80 μm. This relatively small volume of the material potentially reduces the risk of postoperative infection.

Preoperatively all patients gave informed consent to undergo the respective neurosurgical procedures and the clinically indicated routine follow-up exams. Due to the retrospective nature of reporting clinical data only, a special ethics votum was not considered necessary after a respective discussion.

Clinical application
The patch was used in 25 patients, who underwent intradural neurosurgical procedures and exhibited CSF leakage after dural closure due to circumscribed defects or not watertight sutures. The device was not used in patients with pre-existing CSF fistula in which surgery for dural repair was indicated. It was not used in patients with acute infectious symptoms or in pregnant or breast feeding women. Patients with a history or laboratory evidence of haemostatic abnormality were excluded. The material was used in all other patients matching the above mentioned inclusion criteria. Surgical procedures were retrospectively classified as high risk for CSF fistula, if either cisterns or ventricles were widely opened, if it was revision surgery or procedures in the posterior fossa.

Intraoperative procedure
Primary dural sutures can be performed with different suture types like resorbable or non-resorbable sutures. In our institution, dural closure was routinely performed with silk suture (suture strength 2.0 or 3.0 with continuous or single stitches). No other adhesives, e.g. fibrin glue or medicated sponges covered with fibrin and thrombin were used. After primary dura suture had been completed, the operative site was checked for CSF leakage. If no leaks were detected, the intrathecal pressure was raised to provoke CSF leakage via positive end-expiratory pressure (PEEP) enhancement of 5 cm H₂O for 3 minutes. If no CSF leakage was detected, the dura mater closure was considered to be watertight. If CSF leaks were visible, the area was treated with a section of TissuePatchDural® trimmed to size as necessary. Before application of the material, the site should be dried as much as possible. On application, the blue 'T-Dural' text should be readable by the user, ensuring that the adhesive surface is in contact with the dura, with slight manual pressure applied on the patch with a swab for at least 1 minute. Figure 1 shows two examples (A and B) of operative application of the material.

Following application of TissuePatchDural® (to one or more sites where leaks were visible), the PEEP was raised again. If any CSF leakage was detected, a second application of patch was undertaken. Following treatment, routine neurosurgical closure steps were undertaken.

Postoperative course
Postoperatively, patients were visited daily and wound inspections were routinely performed. Unless there was clinical deterioration, no routine radiological scan was performed. All patients were seen after 3 months for clinical inspection. MRI scans of the cerebrum were available in 10/25 patients.

Results
Patient population and clinical course
TissuePatchDural® was implanted in 25 patients (14 male, 11 female, age range from 17 to 81 years). Six patients were
operated for treatment of epilepsy, 15 patients had brain tumours or metastases, 2 patients had intracranial haemorrhage (one subdural haematoma, one atypical intracerebral bleeding), 1 patient had a cerebral cavernous malformation in the brainstem, and 1 patient had trigeminal neuralgia.

Preoperatively, 11 patients took high dose steroids, 7 patients had radiochemotherapy prior to this surgery. Four patients had been operated before, three of them due to brain tumour. A total of 21 craniotomies were performed supratentorially; the posterior fossa was opened in 4 cases. All patients had balanced general anaesthesia using Isoflurane (Abbott) and Remifentanil (GlaxoSmithKline). Mean operation duration was 3.8 hours (range: 1.5–6 hours). Mean blood loss was 285 ml (range: 0–1000 ml). Thirteen of 25 operations (52%) were considered to be high risk operations for postoperative CSF fistula (including all recurrent operations, infratentorial craniotomies or resective operations in which intraoperative opening of ventricle or CSF filled cisterns were performed).

No patient developed infectious complications. No patient developed new epileptic seizures. No patient experienced delayed wound healing. No other complications were observed in the early postoperative course. Mean hospital stay was 11 days (± 5 days) (see Table I).

**CSF fistula**

Two patients developed a visible and palpable subcutaneous collection of CSF. One of these patients had previously been operated for removal of a glioma. This patient had received cerebral radiation therapy as well as chemotherapy. Intraoperatively, the dura mater was extremely thin. A temporary external lumbar drainage was primarily used to prevent a CSF fistula. In the later course, the patient underwent CSF shunting with ventriculoperitoneal shunt in an external neurosurgical department. However, it remained unclear if, initially, the hydrocephalus triggered the CSF fistula or whether it was due to insufficient dura sealing.

The second patient received an external ventricular drain (EVD) intraoperatively for safety reasons presented with a subcutaneous CSF collection 15 days postoperatively. This patient was treated with needle aspiration of the CSF followed by a compression dressing. It might be possible that presence of and removal of the EVD contributed or triggered the CSF fistula.

**Intraoperative handling/experience**

The dural sealant patch was used by 10 different neurosurgeons in the Department of Neurosurgery at the University of Bonn. Users rated the handling characteristics into four different subjective categories: poor (0 times), satisfied (3 times), moderately satisfied (10 times) and extremely satisfied (12 times). Of the three cases where the user rating was classified as ‘satisfied; three of these operations the dura was extremely thin and friable, and dural closure was considered to be difficult. It is important to note that the handling was never rated as ‘poor’ (see Table I).

**Follow up**

Follow up ranged from 3 to 12 months (mean 4.4 months). Three patients died during the observation period. Of these, one patient died of pulmonary sepsis, one patient with bronchial carcinoma died due to pulmonary embolism. Another patient suffered from progressive cerebral tumour growth and died due to a pulmonary infection. No patient died due to a complication directly linked to the neurosurgical procedure.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Gender</th>
<th>Surgery</th>
<th>High risk (HR)/low risk (LR) postoperative CSF leaka</th>
<th>Location</th>
<th>Surgical handling</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>39</td>
<td>w</td>
<td>Lesionectomy</td>
<td>HR</td>
<td>Insular</td>
<td>Extremely satisfied</td>
</tr>
<tr>
<td>2</td>
<td>79</td>
<td>w</td>
<td>Exirpation of cerebellar haemangioima</td>
<td>HR</td>
<td>Cerebellar</td>
<td>Satisfied</td>
</tr>
<tr>
<td>3</td>
<td>65</td>
<td>w</td>
<td>Exirpation of recurrent glioblastoma</td>
<td>HR</td>
<td>Temporoparietal</td>
<td>Extremely satisfied</td>
</tr>
<tr>
<td>4</td>
<td>67</td>
<td>m</td>
<td>Exirpation of glioblastoma</td>
<td>LR</td>
<td>Frontal</td>
<td>Moderately satisfied</td>
</tr>
<tr>
<td>5</td>
<td>78</td>
<td>m</td>
<td>Exirpation of intracerebral haemorrhage</td>
<td>LR</td>
<td>Frontal</td>
<td>Extremely satisfied</td>
</tr>
<tr>
<td>6</td>
<td>47</td>
<td>m</td>
<td>Exirpation of astrocyoma</td>
<td>HR</td>
<td>Insular</td>
<td>Extremely satisfied</td>
</tr>
<tr>
<td>7</td>
<td>19</td>
<td>m</td>
<td>Amygdalohippocampectomy</td>
<td>HR</td>
<td>Temporomesial</td>
<td>Extremely satisfied</td>
</tr>
<tr>
<td>8</td>
<td>69</td>
<td>w</td>
<td>Exirpation of intracerebral haemorrhage</td>
<td>LR</td>
<td>Frontal</td>
<td>Moderately satisfied</td>
</tr>
<tr>
<td>9</td>
<td>19</td>
<td>m</td>
<td>Lesionectomy</td>
<td>LR</td>
<td>Frontal</td>
<td>Extremely satisfied</td>
</tr>
<tr>
<td>10</td>
<td>59</td>
<td>m</td>
<td>Exirpation of anaplastic oligoastrocyoma</td>
<td>LA</td>
<td>Frontal</td>
<td>Moderately satisfied</td>
</tr>
<tr>
<td>11</td>
<td>68</td>
<td>w</td>
<td>Microvascular decompression</td>
<td>HR</td>
<td>Cerebellar</td>
<td>Moderately satisfied</td>
</tr>
<tr>
<td>12</td>
<td>56</td>
<td>m</td>
<td>Exirpation of cerebellar metastasis</td>
<td>HR</td>
<td>Temporomesial</td>
<td>Extremely satisfied</td>
</tr>
<tr>
<td>13</td>
<td>41</td>
<td>w</td>
<td>Amygdalohippocampectomy</td>
<td>HR</td>
<td>Temporomesial</td>
<td>Extremely satisfied</td>
</tr>
<tr>
<td>14</td>
<td>31</td>
<td>m</td>
<td>Lesionectomy</td>
<td>LR</td>
<td>Temporocipitoparietal</td>
<td>Moderately satisfied</td>
</tr>
<tr>
<td>15</td>
<td>52</td>
<td>m</td>
<td>Exirpation of glioblastoma</td>
<td>LR</td>
<td>Frontal</td>
<td>Moderately satisfied</td>
</tr>
<tr>
<td>16</td>
<td>68</td>
<td>m</td>
<td>Exirpation of metastasis</td>
<td>LA</td>
<td>Temporocipital</td>
<td>Moderately satisfied</td>
</tr>
<tr>
<td>17</td>
<td>17</td>
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<td>Lesionectomy</td>
<td>LR</td>
<td>Frontal</td>
<td>Extremely satisfied</td>
</tr>
<tr>
<td>18</td>
<td>81</td>
<td>m</td>
<td>Exirpation of metastasis</td>
<td>LR</td>
<td>Frontal</td>
<td>Extremely satisfied</td>
</tr>
<tr>
<td>19</td>
<td>33</td>
<td>w</td>
<td>Exirpation of recurrent anaplastic astrocytoma</td>
<td>HR</td>
<td>Temporinsular</td>
<td>Satisfied</td>
</tr>
<tr>
<td>20</td>
<td>36</td>
<td>w</td>
<td>Exirpation of recurrent anaplastic astrocytoma</td>
<td>HR</td>
<td>Frontininsular</td>
<td>Extremely satisfied</td>
</tr>
<tr>
<td>21</td>
<td>77</td>
<td>w</td>
<td>Exirpation of meningioma</td>
<td>LR</td>
<td>Temporobasal</td>
<td>Satisfied</td>
</tr>
<tr>
<td>22</td>
<td>43</td>
<td>m</td>
<td>Exirpation of glioblastoma</td>
<td>LR</td>
<td>Frontal</td>
<td>Extremely satisfied</td>
</tr>
<tr>
<td>23</td>
<td>44</td>
<td>m</td>
<td>Exirpation of cavernoma</td>
<td>LR</td>
<td>Brainstem</td>
<td>Moderately satisfied</td>
</tr>
<tr>
<td>24</td>
<td>73</td>
<td>m</td>
<td>Exirpation of metastasis</td>
<td>LR</td>
<td>Temporal</td>
<td>Moderately satisfied</td>
</tr>
<tr>
<td>25</td>
<td>31</td>
<td>w</td>
<td>Amygdalohippocampectomy</td>
<td>HR</td>
<td>Temporomesial</td>
<td>Extremely satisfied</td>
</tr>
</tbody>
</table>
On clinical examinations, none of these patients displayed any clinical sign of CSF leakage. All surviving patients were seen 3 months postoperatively. No delayed or compromised wound healing was recorded in any patient. Apart from the two cases described in the preceding section, no other subcutaneous CSF collection was observed. No patients reported unspecific disorders such as headache, nausea or fever. No patient developed an infectious complication or new epileptic seizures.

Cranial MRI scans of 18 patients were reviewed for meningeal structures, wound configuration, subcutaneous subclinical CSF collections, cortical structure and possible meningoencephaladhesions. General abnormalities were also recorded. The remains of the device could not be identified on the MRI scans. On the basis that resorption of the material is reported to be substantially complete within ~50 days, this finding was not surprising. No clinically occult subcutaneous fluid collection was seen on the MRI scans. There were no signs of meningoencephaladhesions. Overall, no radiological abnormalities were recorded in any case.

**Discussion**

The necessity to achieve ‘watertight’ dural closure in all procedures is a matter of discussion. Failure to effectively close the native dura mater can be a significant source of postoperative morbidity. To ensure watertight primary dural closure, we utilised a surgical sealant film material in 25 patients to seal the dura mater adjunctively. Thirteen out of 25 procedures were considered to have a high risk of CSF fistula. Overall, postoperative subcutaneous CSF collection occurred in 2 out of 25 patients (8%). In one of these patients, an EVD had been placed for safety reasons and CSF leakage occurred shortly after its removal. In the other patient, the postoperative CSF fistula was most likely due to subclinical hydrocephalus. CSF fistula was effectively treated with ventriculoperitoneal shunt placement. Given the considerable proportion of high risk operations for developing a CSF fistula, the incidence of CSF leakage in this series is lower than it is reported in the literature (12-27%). No patient developed postoperative meningitis. Although the lack of a matched control group limits the impact of our finding, the material seemed to be successful in reducing the risk of postoperative CSF fistula and preventing infections and infection related complications. The completely synthetic nature of this product has to be considered advantageous compared to biologically derived devices. This is of significant impact considering the reported cases of severe infectious complications in cases of surgically transmitted infectious diseases such as Creutzfeld Jakob diseases in the use of lyophilized dura mater substitutes.

Intraoperatively, the sealing of the dura was fast. Surgical handling was simplified by the adhesive characteristics of the patch. This feature also reduced the time to closure. The handling of the product was rated by 10 different neurosurgeons. There was no poor rating and in 12 of 25 cases, the surgeon rating was ‘extremely satisfied’. We recorded no intraoperative complications due to the use of the material. Overall, the sealant efficacy of the material was convincing.

We are aware that there are clear limitations of the case series presented here. The retrospective nature, the relatively small patient cohort and the lack of a matched control group due to the observational character of this report do not allow a more detailed statistical analysis of observational findings. Furthermore, this series was not designed to demonstrate the superiority of the material. However, we showed the safe and effective use of the material.

**Conclusion**

Safety, promising effectiveness and convincing handling features of a new bioabsorbable synthetic dural sealant have been demonstrated in this neurosurgical case series.

**Declaration of interest:** The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

**References**


