Safety and efficacy of a novel polyethylene glycol hydrogel sealant for watertight dural repair

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Object. The authors prospectively evaluated the safety and efficacy of a novel polyethylene glycol (PEG) hydrogel sealant in patients undergoing elective cranial surgery with documented cerebrospinal fluid (CSF) leakage after sutured dural repair.

Methods. The PEG hydrogel sealant was used at 11 different study sites in 111 patients with documented intraoperative CSF leakage after neurosurgical dural repair for a variety of conditions. Intraoperative CSF leakage was either spontaneous or induced by a Valsalva maneuver. Patients were monitored for 3 months postoperatively with physical examinations, clinical laboratory analyses, and diagnostic imaging.

The PEG hydrogel sealant was 100% effective in stopping CSF leakage in all patients. There were no sealant-related adverse events and all clinical outcomes were consistent with expectations for seriously ill patients undergoing prolonged neurological procedures.

Conclusions. The PEG hydrogel sealant provides a safe and effective watertight closure when used as an adjunct to sutured dural repair during cranial surgery.

Key Words • cerebrospinal fluid leak • craniectomy • craniotomy • dural defect repair • polyethylene glycol hydrogel sealant

Cerebrospinal fluid leakage is one of the most challenging and potentially dangerous complications of cranial surgery. Despite advances in neurosurgical techniques and the development of adjunctive methods to repair dura mater defects, the incidence of postoperative CSF leaks after cranial procedures performed using the infratentorial or supratentorial approaches can be as high as 10 to 27%.5,10,11,13,38 A metaanalysis of 14 studies documented a postoperative CSF leakage incidence of 10.6% after resection of vestibular schwannomas using suboccipital, translabyrinthine, or middle cranial fossa approaches.20 In another study in which CT scanning was used to evaluate postoperative subcutaneous and/or subgaleal fluid collections, investigators found the incidence of CSF leakage to be as high as 42%.9

A true watertight seal in neurosurgery remains an elusive goal despite meticulous dura mater closure,13,17,40,41 because the holes produced by surgical needles preclude a completely watertight repair that can withstand significant intracranial pressure changes.1,9,23 If the quality of dural closure is improved, complications associated with CSF leakage, including meningitis, pseudomeningoceles, impaired wound healing, and subgaleal fluid collection, could be reduced.9,37 In several studies, a watertight dural closure prevented CSF leakage and significantly decreased the postoperative occurrence of both positional headaches and pseudomeningoceles.1,24,27 Effectively sealing dural incisions during surgery is therefore important because it may prevent CSF leakage and related complications.9,12

Current methods of dural repair include interrupted sutures (possibly using duraplasty to cover significant dural gaps), adhesives, hemostatic agents, and other preparations not specifically approved by the US FDA for dural sealing. In contrast, the PEG hydrogel sealant used in this study was specifically developed to provide a watertight closure as an adjunct to standard methods of dural repair. The PEG hydrogel sealant system involves spraying a synthetic, bio-compatible, tissue-adherent PEG hydrogel onto sutured dural incisions to prevent CSF leakage.

Abbreviations used in this study: CSF = cerebrospinal fluid; CT = computed tomography; FDA = Food and Drug Administration; PEG = polyethylene glycol.
Polyethylene glycol hydrogel sealant in CSF leakage

We present results from an FDA investigational device exemption study in which we evaluated the safety and effectiveness of a novel hydrogel sealant as an adjunct to sutured dural repair during cranial surgery. The primary efficacy endpoint was to prevent intraoperative CSF leaks after sutured dural repair. The safety evaluation included three months of postoperative monitoring for CSF leaks and adverse events as noted by neurological evaluations, laboratory data, and CT studies.

Clinical Material and Methods

Study Design

This study was a prospective, multicenter, single-arm, clinical investigation of patients who underwent elective cranial surgery. Study inclusion criteria included adult patients undergoing elective cranial Class I (clean wound) procedures according to Centers for Disease Control and Prevention criteria. Patients who had undergone prior surgery in the same area, planned penetration of air sinuses or mastoid cells, or prior or planned chemoradiation or radiation therapy, or who had preexisting hydrocephalus, external ventricular shunts or drains, preexisting infection, a compromised immune system, uncontrolled diabetes, or renal or hepatic dysfunction were excluded. The respective institutional review boards approved the study at each site, and informed consent was obtained from all patients. Preoperative baseline evaluations were performed within 2 weeks of surgery.

Intraoperative inclusion criteria included the inability to create a watertight primary sutured closure due to a spontaneous CSF leak or a leak induced by Valsalva maneuver; a total durotomy equal to or longer than 2 cm; dural margins greater than 3 mm or more from the edges of bone; and a Class I (clean) wound. Patients with dural gaps wider than 2 mm after durotomy closure and those who required synthetic or nonautologous duraplasty materials were excluded. A single-arm study was undertaken because an acceptable control treatment was unavailable, as determined by the FDA. The inclusion of a “standard of care” control group would have resulted in a heterogeneous population, thus compromising the ability to pool the data.

Eligible patients with documented CSF leakage after sutured dural repair were treated with the PEG hydrogel sealant (DuraSeal, Confluent Surgical, Inc., Waltham, MA). After the PEG hydrogel sealant had been applied, patients were assessed for intraoperative CSF leakage from the repaired dura during Valsalva maneuvers that produced average pressures of 20 cm H2O for 5 to 10 seconds. If CSF leakage persisted, a second coating of PEG hydrogel sealant was applied and the Valsalva maneuver was repeated. Patients were allowed only two PEG hydrogel applications. If CSF leakage persisted after the second application, conventional management of the leakage was to be instituted at the surgeon’s discretion. The wounds were closed in layers according to each institution’s standard practice. Subgaleal or subfascial drains were placed by the surgeon as deemed necessary. Prophylactic antibiotic therapy was administered during surgery, and a postoperative course of dexamethasone was prescribed to limit inflammation and swelling. Patients were examined postoperatively within 7 days or at discharge, at 6 weeks (± 2 weeks), and at 3 months (± 2 weeks).

Safety assessments included the incidence of CSF leaks within 3 months after surgery, as determined by the need for surgical intervention to treat a CSF leak or pseudomeningocele, diagnostic evidence of CSF leakage, or clinical evaluation, including a physical examination of the surgical site. Additional safety assessments included the incidence of adverse events and adverse sealant-related events revealed by physical examination, diagnostic laboratory tests, and neurological assessments (including pain and disability). Adverse events were defined as unfavorable and unintended signs (including abnormal laboratory findings), symptoms, or disease occurring during the study, regardless of its relation to the sealant. Adverse events were classified as mild, moderate, or severe. A Clinical Events Committee of three board-certified neurosurgeons independently reviewed adverse events.

Baseline CT images were reviewed for informational purposes, whereas images at the 7-day and 3-month follow-up examinations were compared to identify evidence of subgaleal or extradural fluid collection and any other clinically significant findings. An image marker (calibrator reference) was printed on all CT scans to provide a perspective of size to the reviewing radiologist, and calipers were used to measure extradural thickness. Using the initial (≤ 7 days) postoperative CT image, the thickest portion of the hypodense bed was measured and compared with the corresponding anatomical location at the 3-month follow-up, when complete hydrogel absorption was expected.

Three board-certified neuroradiologists independently reviewed the CT scans.

Patient Population

Of the 132 patients who met enrollment criteria, 21 patients failed to meet the intraoperative eligibility criteria, and therefore 111 patients (76 women, 35 men; mean age 49 years, range 20–75 years) were treated with the PEG hydrogel sealant. A majority of patients (53%) were either current smokers or had a history of smoking. A significant percentage of patients had high (≥ II) American Society of Anesthesiologists Physical Status scores (87% ≥ II, 33% ≥ III), indicating a large number of patients had severe systemic diseases and comorbidities. The most common indications for surgery included resection of malignant or benign tumors (46%), microvascular decompression (18.9%), aneurysms (10.8%), epilepsy (9%), arteriovenous malformations (6.3%), and Chiari malformations (5.4%). These 111 patients constituted the population from which baseline data were derived and safety evaluations performed. A total of 11 separate centers participated, with an average enrollment of 10 patients per center (median seven patients).

Sealant Operation and Mechanism

The sealant is provided as a single prepackaged unit with two syringes containing a PEG diluent and a trilysine amine solution, a vial containing end-modified PEG powder with Food, Drugs & Cosmetics Blue No. 1, and a spraying device. To prepare the sealant, the diluent is injected into the powder vial, and the dissolved PEG/dye combination is drawn into the diluent syringe. When mixed, the PEG/dye and amine solutions polymerize to form a strong hydrogel within 2 seconds without detectable heat evolution and without external energy sources. These solutions are simul-
taneously sprayed onto the dura mater, where they polymerize to form an adherent and flexible hydrogel sealant capable of withstanding elevated CSF pressure.

The PEG hydrogel sealant can be stored at room temperature and can be prepared in 1 to 2 minutes. The blue dye in the dilution helps determine sealant coverage and thickness. The hydrogel retains strength while the dura mater heals and gradually hydrolyzes after 8 weeks. The hydrogel breakdown products, including the PEG molecules, are absorbed and cleared by the kidneys. The synthetic nature of the sealant eliminates any potential for viral transmission or sensitization to animal-derived products. All investigators were thoroughly trained in the use of the DuraSeal system.

Statistical Methods

Data from all 11 investigative sites were combined because the surgery site was not predictive of key safety or effectiveness parameters, as demonstrated by the ability to pool analyses. All clinically relevant variables were tabulated using descriptive statistics. Categorical variables were summarized using frequencies and percentages. For select variables, Clopper–Pearson exact 95% confidence intervals were generated. The Wilcoxon signed-rank test was used to determine statistically significant differences in neurologic assessments between baseline and each follow-up visit. The Stuart–Maxwell test was used to determine statistically significant differences in clinical laboratory evaluations between baseline and each follow-up visit.

Statistical tests were performed using SAS statistical software (Version 8.0; SAS Institute, Cary, NC). Regression analyses were used to create models for predicting pre- and perioperative risk factors associated with postoperative infection. Univariate logistic regression analyses were performed on independent variables to identify clinically important or predictive factors. Multiple regression analyses were then conducted (using either a joint or forward selection technique) in which variables suggested by the univariate analysis ($p < 0.07$) were eligible for inclusion.

**Results**

**Surgical Procedures**

A craniotomy was performed in 90 patients (81%), and a craniectomy was performed in 21 patients (19%). The location of the neurosurgical procedure was infratentorial in 53 patients (48%) and supratentorial in 58 patients (52%). The suboccipital surgical approach was used most frequently (41%), followed by the temporal (18%) and frontal (10%) approaches. The mean length of the durotomy was 7.0 cm (range 2.0–19.0 cm). Autologous duraplasty materials were used in 50 patients (45%), most commonly muscle (22%) and then fascia (14%) and pericranium (10%). The mean duration of surgery (the time between skin incision and closure) was 232 minutes (median 205 minutes, range 45–613 minutes). The duration of surgery was prolonged for a significant proportion of patients; in 38% of patients at least 4 hours was required to complete the surgery and in 92% at least 2 hours was required. Drains were placed in 18% of patients.

**Sealant Application**

Following the primary dural suture closure, a spontaneous CSF leak occurred in 67 (60%) of the 111 patients. The remaining 44 patients (40%) required a Valsalva maneuver to generate a CSF leak. The mean pressure achieved during the baseline Valsalva maneuver was 21.4 cm H$_2$O (range 10.0–40.0 cm H$_2$O). A single PEG hydrogel sealant application was effective in obtaining a watertight closure in 105 patients (95%). Persistent leakage after initial application was present in six patients (5%); one leak (0.9%) was spontaneous, and five (4.5%) were induced by the Valsalva maneuver. All six patients (100%) were treated successfully with a second hydrogel application and did not have a CSF leak after a subsequent Valsalva maneuver.

The number of kits used per patient ranged from one to three (median 1 kit). The mean volume of sealant used in the first application was 4.2 ml (range 1.2–13.0 ml). The mean volume of sealant used in the second application was 3.1 ml (range 1.2–4.2 ml). The combined mean total volume of hydrogel sealant used was 4.4 ml (range 1.2–13.2 ml). At the time of sealant application, 95% of the surgeons rated the sealant device as “easy” or “very easy” to use.

**Sealant Efficacy**

By design, all patients enrolled in the study demonstrated either a spontaneous intraoperative CSF leak or a Valsalva maneuver-induced leak after primary suture closure. After a maximum of two sealant applications no intraoperative CSF leaks were apparent during subsequent Valsalva maneuvers. The PEG hydrogel sealant was therefore 100% effective in creating watertight closures, where none existed previously.

**Sealant Safety**

**Wound Healing.** In the early postoperative period, most patients had some expected local swelling at the incision site. At the 6-week examination, the swelling had resolved in 81% of the patients, and at the 3-month examination, the wounds of all 107 patients (100%) remaining in the study were healed.

**Postoperative CSF Leaks.** Postoperative CSF incisional leaks occurred in one (0.9%) of 111 patients, whereas pseudomeningoceles requiring surgical intervention occurred in three (2.7%) of 111 patients. There were no signs of CSF leaks in 106 (95.5%) of the patients (95% confidence interval 89.8–98.5%). For the five patients with CSF leakage (incisional or pseudomeningocele), the time to first leakage ranged from 7 to 29 days. All CSF leaks were diagnosed within 4 weeks of surgery. Cerebrospinal fluid rhinorrhea or otorrhea was not observed. The rate of incisional CSF leakage for all infratentorial incisions was 1.9% (one of 53 patients), and was 1.7% (one of 58 patients) for supratentorial incisions. All incisional leaks and pseudomeningoceles were treated successfully by percutaneous aspiration, oversuturing, temporary external drains, permanent internal shunts, or a combination of these procedures.

**Computed Tomography Scanning.** The CT scans obtained in 17 of the 111 patients treated with the PEG hydrogel sealant could not be evaluated comprehensively because the examination was incomplete, the patient was lost to follow up, there was unusual or tangential positioning of the craniotomy site relative to the CT-scan axis precluding orthogonal
measurement of the surgical site, or the bone flap had been removed between the postoperative and follow-up scans.

The mean immediate postoperative sealant-bed thickness was 5.7 mm, with a mean follow-up thickness of 1.4 mm at 3 months. Thus, the net reduction of the sealant-bed thickness after the 3-month period averaged 4.3 mm, or 75.4% of the original sealant-bed thickness (Fig. 1).

Adverse Events. One patient died of progression of metastatic melanoma 85 days after surgery, and another died of intractable cerebral edema following resection of a glioblastoma multiforme 30 days after surgery. Both deaths were determined by the principal investigator to have been unrelated to the sealant. Two other patients were lost to follow up.

At no time during the study did unanticipated adverse events related to the PEG hydrogel sealant occur. The majority (88%) of patients reported that the adverse events were not severe. The serious adverse events included deep infections of the surgical site (7.2%); postoperative fever (5.4%); stroke, cerebrovascular aneurysm, or cerebral hemorrhage (4.5%); cerebral edema (3.6%); hydrocephalus (3.6%); and bacterial meningitis (1.8%). A review of all adverse events by the independent Clinical Events Committee showed that the adverse events were consistent with the patient comorbidities and the nature of the procedures, and were not associated with the PEG hydrogel sealant.

A forward multiple logistic regression analysis was performed for deep surgical site infections, evaluating only the independent variables demonstrated by univariate analysis to possibly be associated with infection (p ≤ 0.07 based on univariate methods). These variables included the volume of sealant, duration of surgery, length of durotomy, use of intraoperative shunts or drains, and smoking status. Smoking (p = 0.022) and duration of surgery (p = 0.042) were independent predictors for infection. Eight patients with deep wound infections underwent procedures that lasted more than 2 hours, and six of the eight patients (75%) underwent surgeries that lasted longer than 4 hours. Seven of the eight patients (88%) were smokers or had a recent history of smoking, and six patients (75%) had wound drains, incidental sinus penetration, or both.

Discussion

Obtaining a watertight dural closure is a primary objective of neurosurgical practice. Failure to do so often leads to complications related to CSF leaks including meningitis, poor wound healing, and pseudomeningoceles. Primary surjected dural repairs can leak even when using optimal surgical techniques, especially during posterior fossa procedures. Any adjuvant method that can provide a watertight dural seal may be advantageous and desired. Various substances such as fibrin glue, hemostatic agents, and cyanoacrylates have been used for a watertight dural closure but none are currently approved by the FDA for this indication.

The PEG hydrogel sealant used in this study seems ideally suited to its task as it is nonbiological and therefore does not transmit viruses. The sealant is biocompatible (and therefore does not interfere with healing), absorbable, flexible, and strongly adherent to tissue. The PEG hydrogel sealant was 100% effective in sealing intraoperative CSF leaks. There were no sealant-related adverse events, and all clinical outcomes were consistent with expectations for seriously ill patients undergoing prolonged neurosurgical procedures. Eight patients (7.2%) experienced deep surgical site infections, and two (1.8%) postoperative incisional CSF leaks. The absence of a uniform standard of care precluded an acceptable control group and forced the design to be a single-arm study. Therefore, relevant literature must be considered to place both the clinical results and the adverse event rates in perspective.

Cerebrospinal Fluid Leaks

In the present study, a postoperative incisional CSF leak developed in one (1.9%) of the 53 patients with an infratentorial incision and in one (1.7%) of the 58 patients with a supratentorial incision. Both patients had a recent history of hydrocephalus. The treating investigator acknowledged later that the hydrocephalus in the patient with an infratentorial incision was ongoing at the time of the procedure. Three patients had a pseudomeningocele (2.7%) that required surgical intervention. These results compare favorably with the 4 to 30% reported incidence of postoperative CSF leaks in other large surgical series.

In several studies, the development of CSF leaks has been related to the location of the dural incision. Most authors have indicated that CSF leaks develop most frequently in the dependent portion of the skull base region or posterior fossa, whereas CSF leaks are relatively uncommon after surgery in supratentorial regions. For example, the incidence of CSF leakage ranges from 15 to 28% in posterior fossa procedures. Sawaya and coworkers used multivariate analysis to establish that major regional complications—including CSF leakage—were almost six times more likely to occur in infratentorial procedures (Table 1) than in supratentorial procedures (odds ratio 5.84).

To explore the relationship of CSF leakage to a location in the dura, we compared the postoperative leakage incidence for infratentorial and supratentorial incisions. In this study the 1.9% incidence of infratentorial incisional leaks compares favorably to those in published reports in which the average is 12 to 14% and as high as 27%. In the present study, no CSF leaks followed procedures for vestibular schwannomas. This finding compares favorably with the results of a metaanalysis of acoustic neuroma procedures in which investigators found that leaks occurred in 10.6% of suboccipital, 9.5% of translabyrinthine, and 10.6% of middle cranial fossa surgical procedures (overall rate, 10.6%).

Kumar and colleagues prospectively evaluated the use of a biodegradable dural substitute material in cranial fossa procedures in 167 craniotomies performed for a variety of reasons, including tumor resection, cyst fenestration, microvascular decompression, and aneurysmal clip placement. Postoperative CSF leaks, described as fistulas, occurred in two (1.2%) of 167 patients. In the present study we also found two (1.8%) CSF fistulas in 111 patients. A further comparison with the study conducted by Kumar et al. is limited because those authors did not strictly define the diagnosis of CSF leakage and their patients were only followed up once postoperatively after 6 weeks. However, the leakage incidences were similar despite the higher prevalence of infratentorial procedures in the present study (48%) compared with 32% in the study of Kumar, et al.

Bejiani and coworkers presented the results of a prospective multicenter evaluation of a dural substitute material in...
51 patients treated primarily for Chiari malformations and tumors. A suboccipital approach was used in 72% of patients. Shunts or drainage catheters were placed in approximately 10% of patients. Apparently fibrin sealant was used to seal the dura in about 30% of patients. The incidence of CSF leakage was 2%, although leakage was not defined. Whether pseudomeningoceles were included in the leakage rate is unknown. Follow up was 1 month or less in 15 of the 51 patients.

A report by von Wild provided results of a multicenter evaluation of a dural substitute material in 101 patients undergoing supratentorial (75 patients), infratentorial (20 patients), or thoracic (6 patients) spinal operations. This trial is similar to the present study with respect to the number and type of patients, the clinical diagnosis of leaks, and the distinction between CSF fistulas and CSF leaks. The overall incidence of CSF leakage in the von Wild report (12.9%) was significantly greater than that observed in the present study when pseudomeningocele and incisional leak rates are combined (4.5%, \( p < 0.05 \), one-tailed Fisher exact test), even though most (75%) of their procedures were supratentorial.

Sawamura and coworkers reviewed the surgical records of 509 patients who underwent supratentorial craniotomies, in which 295 patients were treated with a fibrin sealant spray and 214 with other methods of fibrin application. The incidences of postoperative CSF leakage in the two groups were 3.1 and 8.9%, respectively. Although CSF leakage was not defined, all 9 instances of CSF leakage in the fibrin spray group were treated by a subcutaneous needle aspiration with a compression bandage or by lumbar drainage.

Additional published reports have focused on specific pathological conditions that represent subsets of patients in the present study. Levy and colleagues reported an 8% CSF leakage incidence (6% leaks and 2% pseudomeningoceles requiring treatment) in 50 children who underwent minicraniotomy for fenestration of temporal arachnoid cysts. In an evaluation by Sarma et al. CSF leaks occurred in 10.9% of patients undergoing primarily frontotemporal or temporal craniotomies for treatment of nonvestibular schwannomas. Eisenberg and coworkers reported a CSF leakage rate of 7.5% (all requiring treatment) in 40 patients undergoing resection of various benign meningeal tumors of the cavernous sinus, primarily using a supratentorial approach.

In the present study, 21 patients underwent craniectomies. In this patient subset, no postoperative CSF leak or pseudomeningocele developed. This incidence rate is much smaller than that observed by Gnanalingham and coworkers, who found the incidence of postoperative CSF leakage after craniectomy to be 27%, with 19.6% of the patients experiencing a pseudomeningocele.

In summary, the incidence of CSF leaks in the present study is low compared with those cited in published retrospective and prospective reports involving similar procedures, patients, and CSF leakage definitions.

Surgical Site Infection

In this study, eight patients (7.2%) experienced a deep surgical site infection. Similar to the incidence of postoperative CSF leaks, the only meaningful comparisons of postoperative infection rates are among comparable patients undergoing comparable procedures.

A meaningful comparison can be made between the present study and one of the largest prospective studies of neurosurgery-related sepsis. As reported by Narotam and colleagues, 2249 neurosurgical patients were evaluated for postoperative infections. Patients were monitored for sepsis.
Polyethylene glycol hydrogel sealant in CSF leakage

<table>
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<tr>
<th>Authors &amp; Year</th>
<th>No. of Patients</th>
<th>Focus of Evaluation</th>
<th>CSF Leak Rate (%)</th>
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<tr>
<td>Patir &amp; Banerji, 1990</td>
<td>179</td>
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<td>26</td>
<td>CM-I via suboccipital craniotomy</td>
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<tr>
<td>Narotam et al., 1995</td>
<td>67</td>
<td>not specifically described</td>
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<td>Anson &amp; Marchand, 1996</td>
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<td>various lesions (meningioma, CM-I, TN)</td>
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<tr>
<td>Mathies et al., 1996</td>
<td>134</td>
<td>PF meningeomas related to the CPA</td>
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<td>Vanaclocha &amp; Saiz-Sapena, 1997</td>
<td>26</td>
<td>CM-I, cadaveric dura vs occipital pericranium &amp; fibrin sealant group</td>
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<td>66</td>
<td>CM-I, duraplasty w/DuraGuard</td>
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<td>Gnanalingham et al., 2003</td>
<td>84</td>
<td>PF tumors</td>
<td>16.0</td>
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* The CSF leak rates were calculated from the referenced papers based on the CSF leak definition used in the current protocol. Abbreviations: CM-I = Chiari malformation Type I; CPA = cerebellopontine angle; PF = posterior fossa; TN = trigeminal neuralgia.

postoperatively until discharge, for 4 weeks after surgery (if the patient remained in the hospital), or when the patient returned for follow-up visits. The definition of surgical site infection was based on Centers for Disease Control and Prevention criteria, but the authors also characterized the types of implants (shunts, drains, or other objects in place for more than 24 hours) and surgery lasting longer than 2 hours, which was then classified as clean contaminated.

The infection rate strongly correlated with the duration of the surgical procedure in the study of Narotam and colleagues. The infection rate for clean surgery lasting more than 4 hours was 13.4%. In contrast, the infection rate for 2- to 4-hour clean surgery was 5.6%. The rate for clean surgery with an implanted foreign body (including wound drains) was 6%. Finally, the rate for clean surgery (exclusion of all known factors that influence sepsis) was 0.8%. These results are similar to data from the study performed by Korinek, in which the infection rate was 32.5% for patients with surgery lasting longer than 4 hours and the overall infection rate was 4.0%. A similar correlation between the incidence of infection and prolonged surgery was observed in the present study, as noted in the results.

Known risk factors were abundant in patients in whom infections in this study developed. Most of the investigational sites were teaching hospitals to which a surgical population requiring complex and prolonged surgical procedures was referred. When compared with surgical procedures of a similar complexity in similar patients, the infection rate in this study is consistent with expected rates from the literature.

Computed Tomography Scanning

Immediately after surgery the PEG hydrogel sealant was hypointense on CT imaging, reflecting its high water content (> 90%). These results are consistent with those of preclinical studies in which this product was evaluated using magnetic resonance and CT imaging in a canine cranio- tomy model. The average cranial space occupied by the infection was 5.7 mm immediately after surgery to 1.4 mm at 3 months. The sealant is reabsorbed within 8 weeks, and therefore the thickness measured at 3 months is probably a combination of thickened dura and fibrous tissue that filled the void as the sealant was absorbed. These findings support claims of sealant absorption within several months.

Conclusions

In patients with demonstrated CSF leaks after sutured dural closure, the novel PEG hydrogel sealant used in this study provided a 100% watertight seal in all patients. The exceptionally low overall postoperative incidence of incisional CSF leakage (1.8%), combined with the 0% leak incidence in cranietomies, supports the hypothesis that intraoperative suture line sealing with this PEG hydrogel sealant should decrease the incidence of postoperative CSF leak. When compared with data from published reports of postoperative CSF leakage among comparable patients and procedures (supratentorial and infratentorial approaches), the results of this study show that the sealant provided a substantial benefit by preventing postoperative CSF leaks after elective craniotomy and cranietomy. Based on the data presented, DuraSeal provides a safe and effective watertight closure when used as an adjunct to sutured dural repair during cranial surgery.

Disclosure

All investigative sites were provided with grant support from Confluent Surgical, Inc. Dr. Robert Spetzler held a significant equity interest in Confluent Surgical at the time of the study. Craig Van Horne, M.D., Kai Frerichs, M.D., and Robert Friedlander, M.D. served as paid consultants to Confluent Surgical, Inc., as members of the Clinical Events Committee. The three neuroradiologists who reviewed CT images—Russell A. Blinder, M.D., Amir A. Zamani, M.D., and Alex Norbash, M.D.—served as paid consultants to Confluent Surgical, Inc., for these services. Dr. Norbash was also employed as a company scientific advisor. All financial interest information was submitted to the FDA.

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