A Novel Impermeable Adhesive Membrane to Reinforce Dural Closure: A Preliminary Retrospective Study on 119 Consecutive High-Risk Patients

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Key words
- Cerebrospinal fluid leak
- Dural repair
- Dural sealant
- Duraplasty
- TissuePatchDural

Abbreviations and Acronyms
CSF: Cerebrospinal fluid
TPD: TissuePatchDural

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OBJECTIVE: **Postoperative cerebrospinal fluid (CSF) leak in neurosurgery remains a significant source of morbidity. TissuePatchDural (TPD), a novel impermeable adhesive membrane, can be used to reinforce dural closure in cases considered at high risk to develop postoperative CSF leak.**

METHODS: **A retrospective, single-center, clinical investigation was conducted on 119 patients who underwent elective neurosurgical procedures between January and June 2010. Inclusion criteria included adult patients undergoing clean elective surgeries where a primary watertight closure was not possible. Three groups of patients were considered: 1) infratentorial, 67 cases; 2) supratentorial, 34 cases; and 3) spinal, 18 cases. All these patients received TPD to reinforce dural closure. Preoperative (long-term corticosteroid therapy, previous surgery and radiotherapy), intraoperative (site of procedures and size of dural gap), and postoperative (early and late hydrocephalus) conditions were analyzed as possible risk factors associated with CSF leakage.**

RESULTS: **The mean follow-up was 7.14 months (range 6–12 months). CSF leak was detected in 11 of 119 cases (9.2%). The presence of pre- and postoperative risk factors was associated with a higher percentage of CSF leakage: 8 of 22 cases (36.3%) vs. 3 of 97 cases (3.1%) ($P < 0.0001$). All leaks could be conservatively treated and no patient required readmission or second surgery. No TPD-related adverse or allergic effects were observed.**

CONCLUSIONS: **TPD seems to be a safe tool to be used to reinforce dural closure in patients with a high risk of developing CSF leaks.**

INTRODUCTION

Cerebrospinal fluid (CSF) leakage is one of the most common and potentially dangerous complications in neurosurgery. Current first line treatment aims to promote wound healing by reducing CSF pressure (CSF lumbar drainage or repeated spinal taps) and to prevent infections by administrating intravenous antibiotics to the patient. Failure of these treatments eventually leads to further surgical procedures. However, in spite of all these treatments, an infection of the CSF itself or of the brain can complicate the postoperative course (8). Although technologic advances in neurosurgical techniques reduced the occurrence of this complication, postoperative CSF leakage is still a serious unsolved problem whose incidence can be as high as 42% (2, 3, 5, 7, 9, 11, 13, 14, 18, 24-27, 29, 30, 33-35, 37, 41).

TissuePatchDural (TPD) (Tissuemed Ltd., Leeds, United Kingdom) is a sterile, self-adhesive, absorbable surgical sealant indicated for adjunctive prevention of CSF leakage in neurosurgery (12). In this retrospective, nonrandomized, single-center study, the authors aimed to evaluate the safety and to obtain initial data about the effectiveness of this novel sealant as an adjunct to standard dural closure during neurosurgical procedures at high risk of developing a CSF fistula.

MATERIALS AND METHODS

Patient Population

This study is a retrospective, single-center, clinical investigation conducted on 119 patients who underwent elective neurosurgical procedures in a 6-month period (January-June 2010). Informed consent was obtained from all patients. Preoperative inclusion criteria included adult patients undergoing clean elective surgeries. Previous radiotherapy, previous surgery, or long-term corticosteroid therapy were not considered exclusion criteria. Intraoperative inclusion criteria included wide cisternal and/or ventricular opening and the failure to obtain a watertight primary closure with a standard dural microsuture (leakage evidenced by subdural irrigation of the surgical cavity before tying the last stitch, followed by Valsalva maneuver to test the last stitch). These patients received TPD to reinforce dural closure. In the period between January and June 2010, a total of 123 consecutive patients treated at the authors' institution were selected as meeting the inclusion criteria described above. Three patients were excluded because of hemorrhagic or ischemic complications that required early reoperation and subsequent TPD removal. One patient was excluded because of a technical problem during the intraoperative application of TPD. In total, 119 patients, 64

Table 1. Surgical Site and Number of Cerebrospinal Fluid Leakage in the 119 Cases Operated at the Fondazione IRCCS Istituto Neurologico Carlo Besta of Milano, Italy, Between January and June 2010, where TissuePatchDural was Used

	Number of Cases (%)	Number of CSF Leaks (%)
Infratentorial craniotomies	67 (56.3)	6 (8.9)
Supratentorial craniotomies	34 (28.6)	3 (8.8)
Spinal cases	18 (15.1)	2 (11)
Total	119	11 (9.2)

CSF, cerebrospinal fluid.

females and 55 males (mean age of 52 years, range 24–82), were analyzed. Within these patients, the following three groups were considered: 1) infratentorial craniotomies, 67 procedures; 2) supratentorial craniotomies, 34 procedures; and 3) spinal cases, 18 procedures (**Table 1**). In addition, patients were stratified according to the presence of 1) preoperative risk factors, including (a) long-term corticosteroid therapy, (b) previous surgery, and (c) radiation therapy; 2) intraoperative risk factors, including (a) durotomy site (supratentorial, infratentorial, spinal) and (b) size of dural gap (CSF leakage only on Valsalva maneuver, small gap (<5 mm) plugged with muscle or collagen, need for duroplasty); 3) postoperative risks factors, including (a) early and (b) late postoperative hydrocephalus (**Tables 2, 3**).

All patients underwent daily postoperative wound examination in order to assess the occurrence of subgaleal CSF collection, incisional CSF leak, any inflammatory reaction or wound infection. An early, usually day 1, postoperative brain or spine computed tomographic scan was performed to detect the development of hydrocephalus or spinal soft tissues CSF collection. In case of clinical uncertainty, a biochemical testing for transferrin was performed in order to confirm CSF leak. The wound was then examined at two weeks and at two and six months after surgery. In addition, in the period from 2 weeks to 2 months, patients were instructed to contact the hospital in case of wound leakage and/or subgaleal or spinal collection. Demographic data, operative and outcome data were collected and analyzed.

In this study the term "CSF leak" was used for both pseudomeningocele and incisional CSF leak. The etiology of these complications is the leak of the CSF from the subarachnoid space to the extradural compartment. When the skin incision has adequately healed, a pseudomeningocele may develop; otherwise, an incisional CSF leak can also occur. However, both situations should be considered as a failure of the dural sealant to prevent CSF from leaking to the extradural compartment (38).

TissuePatchDural

TPD is a sterile, self-adhesive, absorbable surgical sealant and barrier available in four different sizes ranging from 25 × 50 mm to 10 × 100 mm (**Figure 1**). It is a multilayered device comprising alternate layers of poly(lactide-*co*-glycolide) and a proprietary adhesive Terpolymer. Poly(lactide-*co*-glycolide) is a resorbable membrane that provides reliable strength for temporary wound support (12).

According to the product instructions for use provided by the manufacturer (Tissuemed Ltd.), the material is adhesive by virtue of the initial tack provided by both poly(acrylic acid) and poly(vinyl pyrrolidone) functional groups and longer term adhesion via nucleophilic substitution reaction between N-hydroxysuccin-

Table 2. Comparison of Studies with Different Types of Dural Sealant Including the Present

Author	Sealant	Number of Patients	% of Leakage	% High-Risk Patients	Site	Follow-Up Period (months)
Boogaarts et al., 2005 (4)	DuraSeal	46	4.9% (out of 41 patients)	High- and low-risk procedures	26 supratentorial 18 infratentorial 2 spinal	3
Cosgrove et al., 2007 (8)	DuraSeal	111	4.5%	High- and low-risk procedures	58 supratentorial 53 infratentorial	3
Than et al., 2008 (38)	DuraSeal	100	2%	Not specified	Posterior fossa	2.9
Kumar et al., 2003 (22)	Bioglue	210	0.93% (in two posterior fossa approach)	Not specified	114 supratentorial 53 infratentorial 41 transsphenoidal 8 spinal	1.5
Jankowitz et al., 2009 (21)	Tisseel	278	11.9%	Not specified	Spine	3
Ferroli et al., 2011 (current study)	TissuePatchDural	119	9.2% (11 of 119) 36.3% (8 of 22) of high-risk cases* 3.1% (3 of 97) of normal-risks cases†	All patients with wide cisternal or ventricular opening. 22 of 119 (18.5%) high-risk cases*	67 infratentorial 34 supratentorial 18 spinal	6

*Patients with preoperative (previous surgery, radiotherapy, and long-term corticosteroid therapy) and postoperative (early and late hydrocephalus) risk factors.
†All the other patients.