Influence of TachoComb® in Comparison to Local Hemostytic Agents on Epidural Fibrosis in a Rat Laminectomy Model

Abstract

This animal experimental study was designed to examine the effects of TachoComb®, a fixed combination of collagen with tissue adhesive, as an interposition membrane on the development of spinal epidural fibrosis in comparison to other hemostytic materials. In 10 Wistar rats, four laminectomies were performed at lumbar and sacral vertebrae. Alternately, a piece of TachoComb®, Spongostan®, or Tabotamp® was placed into each laminectomy site. One laminectomy site served as an empty control (n = 10). 8 weeks later, the animals were sacrificed, and the spinal column including surrounding muscle tissue was removed en bloc from each rat and fixed in formaldehyde. After decalcification and staining the specimens were graded by a neuropathologist in a blindfold test for severity of epidural fibrosis as “light-moderate” or “marked”. Epidural scarring of variable density was seen in all laminectomy sites. Light epidural fibrosis, without any adhesion to dura, as only noted in cases after application of TachoComb® (n = 4/10) and Spongostan® (n = 1/10). All other slices showed marked epidural fibrosis with dura adherence regardless of the implanted material. Statistical analysis revealed significantly lower epidural fibrosis after application of TachoComb® compared to all other groups (p < 0.05). In this series, TachoComb® is more effective in reducing the epidural fibrosis than Spongostan® and Tabotamp®. However, complete prevention of scar tissue formation was not achieved.

Key words

Epidural fibrosis · failed back surgery syndrome · interposition membrane · hemostystica

Introduction

Every year over one million patients worldwide undergo lumbar-sacral surgery for disc herniation [1]. Despite improvements of surgical techniques as well as the adoption of microsurgical approach, the failed back surgery syndrome represents with an incidence of 5 – 10% a major problem in spinal surgery [1 – 4]. The formation of postoperative epidural fibrosis with nerve root entrapment and dural compression is said to be the most common cause [5]. Since – because of scar recurrence – scar excision surgery generally yields poor results [6,7], many authors have suggested that prevention of postoperative adhesions is an essential goal in lower back surgery [2].

In the last years, a number of investigators have studied the effectiveness of various treatments for preventing epidural fibrosis with variable success [4,6,8 – 13].

TachoComb® (Nycomed, Ismaning, Germany) is a local hemostytic agent consisting of a patch of collagen which is covered with a fixed layer of the solid coagulation factors fibrinogen and thrombin and fibrinolysis inhibitor aprotinin. Its hemostytic properties are superior to Gelfoam® and Tabotamp®.

Based on the theory that the peridural fibrosis after lumbar laminectomy and discectomy is resulting primarily from the damaged erector spinae muscles and the hematoma forming in the path of the surgical dissection, we examined the effects of TachoComb® as an interposition membrane on the development of spinal epidural fibrosis in comparison to other hemostytic agents in a rat laminectomy model.
Material and Methods

The experiments were carried out on 10 adult Wistar rats. The animals were anesthetized with intraperitoneal application of Nembutal (7.5 mg/kg BW). The animals were positioned prone on a heating blanket. The temperature was kept constant at 38 ± 0.4 °C, controlled by the rectal temperature. With the aid of a surgical microscope and using an aseptic technique, four laminectomies were performed in each animal at lumbar and sacral vertebras. The dorsal skin and fascia were incised in the midline. After separation of the paraspinal muscles the spinous processes were removed with a rongeur. The laminectomy defect was created with a high-speed drill to an approximately rectangular size of 3 × 2 mm. Every other lamina between two laminectomy sites was left in place. After hemostasis with bipolar cautery, a piece of TachoComb®, Spongostan®, and Tabotamp® was placed alternately into the laminectomy site. One laminectomy site served as an empty control. The wound was closed in layers. 8 weeks postsurgery the animals were sacrificed by intraperitoneal application of a lethal dose of Nembutal (75 – 100 mg/kg). The spinal column, including surrounding muscle tissue, was removed en bloc and fixed in 10% formaldehyde at room temperature. After decalcification with 2 M HCl, the specimens were embedded in paraffin and stained with hematoxylin, eosin, and van Gieson for light microscopic examination.

The preparations were investigated for severity of epidural fibrosis detecting dural adhesions, mononuclear infiltrations, vascularizations, fibroblast activities, neighbouring muscle and bone tissue changes. The epidural fibrosis was classified in a blindfold test on a subjective scale by a neuropathologist regarding tissue scar density as “light–moderate” or “marked” (Figs. 1–4).

Results

The postoperative course was uneventful in all animals. No incidence of wound infection or abnormal foreign-body reaction could be detected.

Fig. 1 Control laminectomy site (H&E, original magnification × 2.5). Laminectomy defect filled with dense epidural fibrosis with marked dural adhesion.

Fig. 2 Tabotamp®-implanted laminectomy site (H&E, original magnification × 5). Laminectomy defect filled with dense epidural fibrosis. Cellular density, marked dural adhesion. Sinusoidal venous vessels on the left side.

Fig. 3 Spongostan®-implanted laminectomy site (H&E, original magnification × 5). Laminctomy defect filled with dense epidural fibrosis with marked dural adhesions.

Fig. 4 TachoComb®-implanted laminectomy site (H&E, original magnification × 5). Loosely arranged fibrosis, sharply demarcated from the dura. Sinusoidal vessels.
Histological analysis revealed variable intensity of epidural scar formations with different dural adhesions in all laminectomy sites. In all cases, the laminectomy site was filled out with scar tissue, which arose from the overlying paraspinal musculature. The epidurally implanted materials were already completely resorbed. The scar formation, directly adjacent to the paraspinal musculature and bony structures, showed the strongest density. In four cases with TachoComb® and one case with Spongostan®, only light epidural scar tissue without any adhesion to dura was noted. All other slices showed a marked epidural fibrosis. The statistical analysis (Fisher test) revealed significant differences between the TachoComb®-implanted sites and the other groups (p < 0.05) (Table 1).

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<th>Table 1</th>
<th>Extent of epidural fibrosis</th>
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Discussion

The development of failed back surgery syndrome after lumbar laminectomy and discectomy is frequently caused by the development of a significant epidural fibrosis with nerve entrapment and dural compression. Possibly, nerve root atrophy and extradural or intradural fibrosis leads to an increase in mechanical sensitivity and reduction of nociceptor threshold. Because scar excision surgery generally yields poor results, it is essential to distinguish recurrent disc herniation from postoperative scar formation. Computed tomography and magnetic resonance imaging, with intravenous contrast, are effective in distinguishing recurrent disc herniation from scar tissue [14].

Numerous investigators have searched for various agents acting as a barrier to the formation of peridural adhesions with different results [10,11,15]. While LaRocca and McNabb concluded that Gelfoam as well as a Silastic membrane were effective as barriers in limiting scar tissue [12], most subsequent authors described that Gelfoam increases scar tissue formation [4,10,16–19]. A most effective barrier appears to be an implant of fat graft over the laminectomy site [10]. Using a free epidural fat graft as interposition membrane can cause severe complications secondary to migration of the graft [20,21]. In addition, hyaluronic acid and GL 402 were effective in reducing scar formation, both substances act by preventing the invasion of fibroblasts [13,15]. However, the latter mentioned agents have no hemostytic properties. The results of a prospective clinical study indicate that epidural placing of Gelfoam or free fat graft had no effect on patient outcome regarding symptoms, functional status, and magnetic resonance imaging findings [22]. Even if epidural fibrosis may be less likely a cause of failed back surgery syndrome, an effective material acting as an interposition membrane facilitates surgery of recurrent disc herniation.

In spinal surgery, the surgeon is often confronted with epidural bleeding from the venous plexus. In the later course, the clot formation is absorbed and gradually replaced by granulation tissue maturing into a dense fibrotic tissue. Efforts on reducing scar formation should concentrate also on reducing hematoma formation, the first stage in the development of fibrosis [15].

TachoComb®, a local hemostptic agent consisting of a patch of collagen which is covered with a fixed layer of the solid coagulation factors fibrinogen and thrombin and the fibrinolysis inhibitor aprotinin, proved to reduce risk of postoperative cerebrospinal fluid leak as well as infection after skull base procedures [23]. The gluing properties of TachoComb® showed to be convincing, according to preclinical trials published by Schelling et al. [24]. It has been used very successfully in surgery of parenchymatous organs (liver, spleen, pancreas, lung, kidney, and thyroid gland) [25]. So far, no reports have been published about the application of TachoComb® in spinal surgery procedures. Because of its hemostytic and gluing qualities, it could be a very useful adjunct, especially in cases of dural lesions with the risk of postoperative CSF leak. Thus, we have compared TachoComb® with other hemostytic materials regarding the formation of epidural fibrosis in a rat laminectomy model before using the agent routinely in spinal surgical procedures.

In agreement with other investigators, all implanted groups show less dense epidural fibrosis than control laminectomy sites without any implants [4,9–13,15,20,22]. TachoComb® was more effective in reducing the epidural fibrosis than Spongostan® and Tabotamp®, but complete prevention of scar tissue formation was not achieved. Our results show that TachoComb® seems to be a useful adjunct in spinal surgical procedures.

References