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Topical high-molecular-weight hyaluronan and a roofing barrier sheet equally inhibit postlaminectomy fibrosis

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Abstract

BACKGROUND CONTEXT: The relevance of epidural fibrosis to failed back surgical outcomes remains controversial. Previous studies on the correlation between epidural fibrosis and clinical outcome after laminectomy are inconclusive, and clinical approaches applied to reduce postlaminectomy spinal canal scarring have produced mixed outcomes.

PURPOSE: Improved preclinical models are required to address the fundamental question of the relationship between postlaminectomy fibrosis and chronic pain. This study is directed at establishing small animal postlaminectomy models characterized by significantly reduced scar within the spinal canal postoperatively. Such preclinical models are offered as a platform for future studies to explore the potential relationship between postlaminectomy epidural fibrosis and persistent neuropathy with its potential for altered spinal mechanisms for pain processing, so-called spinal facilitation. Such experiments could be constructed in these models for comparison of pain behavior and its underlying neurochemistry both in the presence and absence of extensive postlaminectomy epidural scar.

STUDY DESIGN/SETTING: A modified rat laminectomy model was employed to assess epidural fibrosis using a quantitative biochemical collagen assessment approach along with correlative histology. This group served as the control for comparison with groups in which antifibrotic measures were employed. We compared antifibrotic efficacy of a bioabsorbable roofing barrier sheet placed over the laminectomy defect with topical high-molecular-weight hyaluronan (HMW HA) gel, each applied postoperatively to prevent proliferative epidural scarring. Routine biomechanical tensile strength testing was employed to assess wound-healing strength.

METHODS: A bilateral laminectomy (L5 and L6) with associated unilateral disc injury (L5–L6) was performed in 98 male Harlan Sprague-Dawley rats. The laminectomy models described incorporated a unilateral disc injury at L5–L6 because herniated disc material has been shown to contribute proinflammatory cytokines in the postoperative wound. Five groups were employed for the study: 1) normal controls without surgery; 2) a laminectomy-disc injury group without treatment; 3) a laminectomy-disc injury group treated with topical HMW HA gel; 4) a laminectomy-disc injury group treated with 0.2-mm thick bioabsorbable roofing barrier sheet in which a protected space was maintained between overlying paraspinous muscles and the dura and 5) a 0.02-mm thin barrier sheet treatment group in which the sheet was placed directly on the dura. The animals were sacrificed at 3- and 8-week postoperative intervals for analysis. The dissected specimens were studied biochemically for hydroxyproline content to estimate total collagen within the canal and on the dura between L4 and L7. Additional specimens were prepared histologically and stained with Masson-Goldner Trichrome stain to confirm presence of proliferative collagen and to describe the

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presence or absence of wound-healing scar adherence to the dura. The surgical incisions were studied biomechanically by uniaxial tensile testing to determine ultimate force, strain and prefailure stiffness. Statistics were performed using analysis of variance.

RESULTS: Gross appearance and histology studies showed that the untreated laminectomy group demonstrated postoperative scar formation that is adherent between the wound and the dorsum of the dura mater in both 3- and 8-week groups. Proliferative scar was substantially increased grossly between the 3- and 8-week intervals. By gross observation there was adherence of the L5 spinal nerve to the underlying disc and adjacent pedicle on the disc injury side. Gross observation of treatment groups, in contrast, disclosed that both the 0.2-mm thick roofing barrier sheet and topical HMW HA gel each prevented scar attachment to the dural sleeve at both the 3- and 8-week postoperative intervals. Furthermore, both the HMW HA gel and 0.2-mm thick roofing barrier sheet treatment groups had significant reduction of total collagen content in the laminectomy specimens measured biochemically at the two time periods compared with the untreated controls. Histologically, the HMW HA gel and the 0.2-mm thick barrier sheet findings were consistent with the gross observations concerning lack of adherence between scar of the overlying wound and the dura. Notably, both the 0.2- and the 0.02-mm barrier sheets became enveloped by a fibrotic envelope consistent with a foreign body reaction. In the group in which the 0.02-mm thin sheet was placed within the canal on top of the dura, there was an increase of fibrosis around the sheet within the canal leading to a space-occupying mass within the canal. Although the 0.2-mm thick roofing barrier placed external to the canal became enveloped by scar, it appeared to attract proliferative scar away from the epidural space, leaving the dura relatively free of scarring or adherence to overlying tissues. The mechanical properties of the incisional wound increased significantly between 3 and 8 weeks. The ultimate strength, stress, strain and stiffness of the several groups were similar at each time point

CONCLUSION: These results provide two preclinical rat laminectomy models of potential usefulness for the future study of the relevance of epidural fibrosis to behaviorally defined pain states, and for the study of the potential of an altered neurochemical signature in postlaminectomy pain conditions. Such preclinical models have become standard in studies of pain behavior and its neurochemistry in preclinical sciatic nerve and spinal nerve injury models, and should be of utility in the studies of postlaminectomy fibrosis. There was progressive scar proliferation and maturation in the untreated postlaminectomy group in the postoperative interval between 3 and 8 weeks. HMW HA gel applied topically and a 0.2-mm thick bioabsorbable Macropore sheet used as a roofing barrier each significantly reduced postlaminectomy proliferative scar without affecting the integrity of incisional wound healing. However, if the 0.02-mm thin barrier sheet used in this study is placed within the canal in contact with the dura and adjacent to the pedicles, the process of reabsorption results in a fibrotic mass within the canal. The preferred barrier sheet placement for this model is clearly in a roofing position bridging over the open epidural space. It must be placed in a manner to block off the paraspinous muscle healing response and still leave a gap between the sheet and the dura.

Keywords: Spine; Laminectomy; Disc injury; Epidural fibrosis; Barrier sheet; HA gel

Introduction

This paper addresses the need for suitable preclinical models for the study of the consequences of proliferative fibrosis within the spinal canal after laminectomy.

Lumbar discectomy is one of the most common surgical procedures used in treatment of spinal disorders [1,2]. Numerous authors report overall good and excellent results from the procedure. In prospective randomized series, the success rate is between 70% and 86% [3–6]. However, prospective evaluation clearly shows that many people continue to have significant pain and disability after lumbar disc surgery. In the study by Atlas et al., 19% of surgical patients undergo at least one additional spine operation by 5 years [7,8]. Asch reported that only 65% of patients return to normal daily activities and only 61% return to work after spine surgery [4].

Epidural/peridural/perineural scarring is commonly attributed to many of the surgical failures [9]. The clinical consequences of neural scarring is well described in numerous other areas of the body, including the carpal tunnel, tarsal tunnel and brachial plexus where inflammation, swelling and fibrosis can lead to chronic neurogenic pain [10–19]. The analogy of nerve entrapment syndromes to the postlaminectomy fibrosis process seems compelling. Furthermore, with the advent of magnetic resonance imaging (MRI), it is known that proliferative scarring occurs frequently after spine surgery [20–22]. However, the majority of clinical outcome studies employing MRI assessment of postlaminectomy scarring have found no correlation between the MRI assessment of scar within the spinal canal and chronic pain [22–24]. While there is no doubt that epidural scarring often makes repeat laminectomy surgery more difficult and adds to the complication rate, there is also no