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The Spine Journal 5 (2005) 479–488

THE SPINE JOURNAL

Clinical Studies

Evaluation of hyaluronic acid sheet for the prevention of postlaminectomy adhesions

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Received 20 October 2004; accepted 26 January 2005

Abstract

BACKGROUND CONTEXT: Various materials have been tested for their ability to maintain a barrier between muscles and epidural space in order to physically or chemically inhibit scar ingrowths. Hyaluronic acid (HA) solution and gel have been reported to be effective in preventing adhesions postlaminectomy; however, neither has been used clinically after spinal surgery.

PURPOSE: To determine the efficacy of HA sheet for the prevention of postlaminectomy adhesions compared with that of HA gel or another sheet.

STUDY DESIGN/SETTING: An animal model of lumbar laminectomy in rabbits was used to study postoperative scar tissue formation around the spinal cord. The histologic effects of HA sheet were compared with those of Gelfoam (GF) and further evaluated by an inflammation model using rhTNF-α.

PATIENT SAMPLE: Rabbit.

OUTCOME MEASURES: Histologic examination.

METHODS: Five rabbits were killed at 2, 4, 8, and 24 weeks after laminectomy, respectively. Another 18 rabbits were examined in an environment of active inflammation experimentally induced by rhTNF-α to compare the effects of HA sheet with those of GF or HA gel. Histologic examination was performed to quantitatively assess invasive scar formation or inflammation postlaminectomy, and then, the histologic effects of HA sheet were compared with those of GF or HA gel.

RESULTS: In the HA group, significantly, the area of subarachnoid space was larger, distance from the surface of dura to scar tissues was greater, the number of inflammatory cells in the scar tissues at the site of laminectomy was less, and enlargement of dura was suppressed. Using an inflammation model, we also demonstrated the efficacy of HA sheet treatment.

CONCLUSIONS: In an experimental laminectomy model, HA sheet formed a solid interpositional membrane barrier and exhibited anti-inflammatory activity. Further investigations will be needed for HA sheet to be used clinically.

Keywords: Hyaluronic acid sheet; Postlaminectomy; Adhesion; Anti-inflammation; Interpositional membrane

Introduction

After lumbar laminectomy, the adhesion of postoperative scar tissue to surgically exposed dura and, occasionally, to nerve roots has been implicated as a possible cause of recurrent radicular or low back pain [1,2]. Furthermore, in the event further surgery is needed, the presence of scar tissue increases the technical difficulty of the operation and also increases the risk of iatrogenic nerve root damage and dural tears [3–5].

In 1974, LaRocca and MacNab [6] reported that the development of epidural scar tissue after laminectomy (the postlaminectomy membrane) resulted from the destruction of epidural fat, intraspinal hematoma, and invasion of the spinal canal by the erector muscles of the spine. Since then, numerous investigators have tested various materials for their ability to maintain a barrier between muscles and the epidural space

FDA device/drug status: investigational/not approved (Hyaluronic Acid Sheet).

Nothing of value received from a commercial entity related to this manuscript.

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1529-9430/05/$ – see front matter
doi:10.1016/j.spinee.2005.01.010

[4,7–27]. In particular, test materials have been placed over surgically exposed dura in an attempt to physically [4,7–21] or chemically [22–27] inhibit scar ingrowths.

Although those studies have had conflicting results, transplanted fat seems to most reliably prevent the formation of an epidural scar [15,16]. There are a number of concerns associated with the use of fat grafts, however, including weakness against applied pressure, the possibility of necrosis, seroma formation, infection, and, in thin individuals, dimpling at the site of harvest. Moreover, some reported fat grafts caused much fibrosis tissue [21,22]. We therefore have been searching for a suitable synthetic substitute for fat grafts as the interpositional membrane.

Prevention of adhesions is a critical concern in all fields of surgery, not just spinal surgery. Experimental studies to prevent adhesions of scar tissues have thus been conducted in non-spinal surgery tissues as well [28–30]. Recently, hyaluronic acid (HA) has been reported to be useful in preventing adhesions and is in clinical use in the field of general surgery [28,29]. Experimental studies have reported that HA has efficacy against postlaminectomy scar formation [25,26], but HA has not been used clinically in the field of spinal surgery.

In the current study, we used a new, synthetic material derived from HA, called HA sheet (Denki Kagaku Kogyo K.K., Tokyo, Japan, patent number US6387413B1) (Fig. 1). HA sheet is a very thin, solid, biocompatible sponge sheet composed of self-cross-linked HA molecules. Its molecular weight is about 20 thousand kDa, and its pore size varies from 50 μm to 200 μm. The purpose of the current study was to investigate the efficacy of HA sheet as an interpositional material to suppress postlaminectomy scar invasion.

Materials and methods

Animals

The Animal Care Committee of Tokyo Medical and Dental University approved all experimental protocols used (No. 0040243). Twenty Japanese white rabbits (female, age 20–30 weeks, weight 2–3 kg; Sankyo Laboratory, Tokyo, Japan) were used.

Surgical procedure

After the animals were anesthetized intravenously with sodium pentobarbital (Nembutal; Dainippon Pharmacy, Osaka, Japan, 0.5 mL/kg), they were placed on the table in the prone position. A midline incision was made posteriorly in the lumbar region, and three separate laminectomies (10×6 mm size) were performed at lumbar vertebrae L1, L2, and L3. Each of the three laminectomy sites was treated differently: (a) the defect was left empty and covered by reapproximation of soft tissue and skin (control group); (b) Gelfoam (GF) (Sumitomo Pharmacy, Tokyo, Japan), a resorbable gelatin foam sponge that has been used clinically as a barrier membrane after laminectomy, was cut to suitable size and placed over the defect (GF group); (c) HA sheet was cut to suitable size and placed over the defect (HA group). The control and implant sites were randomly assigned in each animal to diminish the influence of any level-specific variations. A standard closure was performed for all animals. Postoperatively, the rabbits were housed in individual cages and allowed normal activity.

Histologic examination

Five rabbits were killed at 2, 4, 8, and 24 weeks after laminectomy, respectively. The lumbar spines were removed

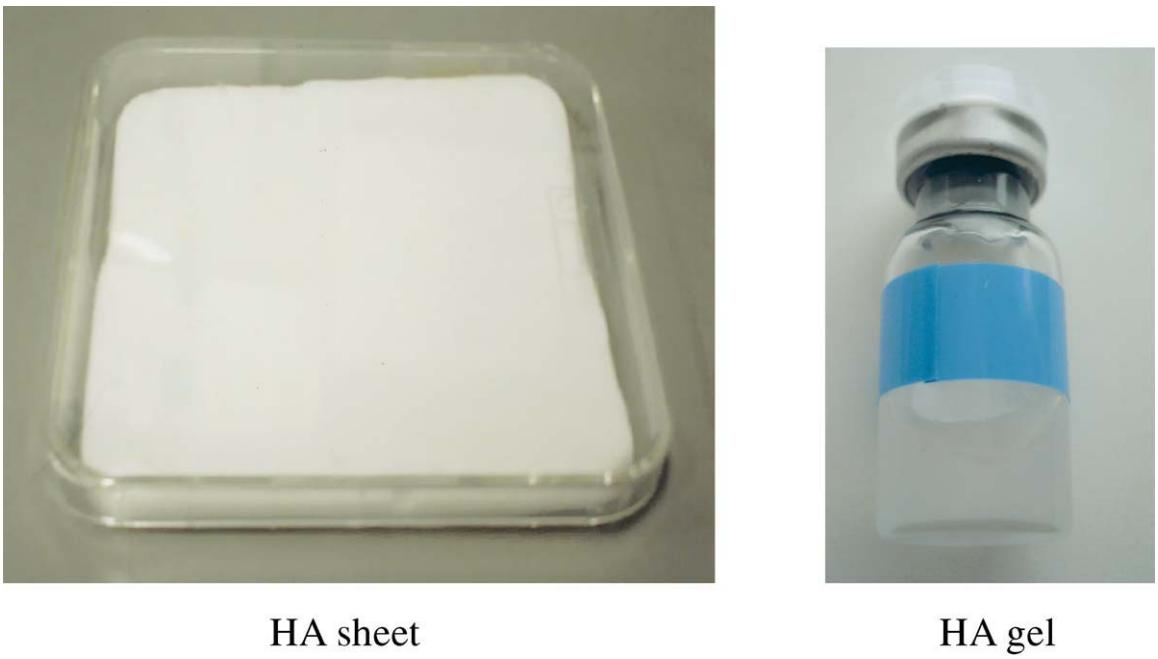

Fig. 1. Hyaluronic acid (HA) sheet (left) and HA gel (right) are shown. Both have been developed by Denki Kagaku Kogyo, K.K., patent number US6387413B1.