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Basic Science

The anabolic effect of plasma-mediated ablation on the intervertebral disc: stimulation of proteoglycan and interleukin-8 production

Fabrice A. Kuelling, MD[a], Kevin T. Foley, MD[b], Jane J. Liu, MD[a], Ellen Liebenberg, BS[a], Anthony H. Sin, MD[b], Akihiro Matsukawa, MD, PhD[c], Jeffrey C. Lotz, PhD[a,*]

[a]*Orthopaedic Bioengineering Laboratory, Department of Orthopaedic Surgery, 513 Parnassus Ave, Box 0514, University of California, San Francisco, CA 94143, USA*
[b]*Department of Neurosurgery, University of Tennessee, 427 Johnson Building, Memphis, TN 38119, USA*
[c]*Department of Pathology and Experimental Medicine, Okayama University School of Medicine, 2-5-1, Shikata, Okayama 700-8558, Japan*

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Abstract

BACKGROUND CONTEXT: Plasma-mediated radiofrequency-based ablation (coblation) is an electrosurgical technique currently used for tissue removal in a wide range of surgical applications, including lumbar microdiscectomy. In vitro and in vivo studies have shown the technique to alter the expression of inflammatory cytokines in the disc, increasing the levels of interleukin-8 (IL-8), which may promote maturation and remodeling of the disc matrix.

PURPOSE: To better understand the effect of coblation treatment, this study characterizes the temporal and spatial pattern of healing after stab injury to the rabbit intervertebral disc, with and without plasma-mediated radiofrequency treatment.

PATIENT SAMPLE: A total of 23 New Zealand white rabbits.

STUDY DESIGN: Annular and nuclear stab injuries.

OUTCOME MEASURES: Sandwich enzyme-linked immunosorbent assay evaluated the concentrations of cytokines tumor necrosis factor-α, IL-1β, and IL-8. Histopathologic evaluations were performed on whole discs and end plates. Tissue sections were stained with Safranin-O to evaluate nucleus pulposus and annulus fibrosus proteoglycan content and with Alcian blue for extracellular proteoglycan content. Intradiscal leakage pressure was evaluated by injecting methylene blue dye into the nucleus.

METHODS: Animals underwent annular and nuclear stab injuries on three consecutive lumbar discs (L2–L3 to L4–L5). The three levels were randomly assigned into one of the three groups for treatment with a plasma-mediated radiofrequency ablation device (TOPAZ; ArthroCare Corp., Austin, TX, USA): active treatment of the nucleus only (SN); active treatment of both nucleus and annulus (SNA); sham treatment. Unstabbed/untreated discs from L5–L6 (n=5) served as normal controls. Animals were euthanized at 4, 8, and 28 days postsurgery.

RESULTS: Tumor necrosis factor-α was detected in sham discs at 4 and 8 days, but not in coblation groups (SN or SNA); IL-1β was below detection in all three treatment groups. Interleukin-8 levels increased in all treatment groups at 4 and 8 days compared with normal control, peaking at 4th day for sham and SN groups and 8th day ($p>.3$) for the SNA group (a 2.5-fold increase). Pressure measurements revealed higher leakage in the SN group, but no statistically significant

FDA device/drug status: Approved (TOPAZ, ArthroCare Corp., Austin, TX).

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The disclosure key can be found on the Table of Contents and at www.TheSpineJournalOnline.com.

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* Corresponding author. Orthopaedic Bioengineering Laboratory, Department of Orthopaedic Surgery, 513 Parnassus Ave, University of California, San Francisco, CA 94143-0514, USA. Tel.: 415-476-7881; fax: 415-476-1128.

E-mail address: jeffrey.lotz@ucsf.edu (J.C. Lotz)

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differences. Histopathology showed higher proteoglycan production by 28 days in the SNA and SN groups compared with sham. All three treatment groups showed ruptured annular fibers from the stab injury, but maintained the overall architecture. Remnants of notochordal tissue within the nucleus were evident in all treatment groups at 4 and 8 days, but were only found in sham group by 28 days. At this time, unlike the normal or sham controls, the nucleus of SN and SNA discs had fibrocartilaginous tissue with chondrocyte-like cells. Significant differences in the disc architecture grade were only noted when comparing normal controls with other groups by 28 days ($p<.001$).
CONCLUSIONS: Plasma-mediated radiofrequency ablation appears to have an anabolic effect on disc cells, stimulating proteoglycan and IL-8 production and maintaining annulus architecture. Coblation treatment appears to reduce cellular response to proinflammatory stimuli and restore overall disc architecture that may prove beneficial in a number of degenerative disc paradigms. Further studies are encouraged to investigate the therapeutic effect of the technique.

Keywords: Intervertebral disc; Histopathology; Cell proliferation; Coblation; IL-8; TNF-a; Proteoglycan; Notochordal cells; Annulus fibrosus

Introduction

The intervertebral disc (IVD) is the largest avascular structure in the body, and it fulfills a demanding physical role. Under these circumstances, the limited nutrition hinders matrix synthesis and contributes to the catabolic processes that underlie age-related degeneration. Persistent inflammation may arise when matrix damage outpaces tissue healing [1,2], causing pain and disability. Because the disc is commonly considered the culprit in patients with chronic axial back pain, current surgical treatment strategies involve disc removal followed by fusion or arthroplasty. However, these procedures carry a significant risk to the patient, are costly, and have variable outcomes [3]. Consequently, minimally invasive procedures that encourage disc healing are being sought as an alternative to open surgery for these patients.

Plasma-based bipolar radiofrequency ablation (coblation) is a relatively newly described electrosurgical technique that uses a controlled, nonheat-driven mechanism to ablate soft tissue and stimulates soft tissue healing via a controlled inflammatory process. In brief, coblation uses an electromagnetic field to excite the particles within a conductive solution, such as saline, to create plasma. The highly reactive and energized particles generated by the plasma can selectively interact with tissue molecules through a low temperature etching. This results in volumetric removal of the target tissue with minimal damage to the surrounding tissue. Coblation has been shown to stimulate connective tissue healing at various musculoskeletal sites including tendons, the knee meniscus, and the articular cartilage [4–6]. O'Neill et al. [7] demonstrated that percutaneous plasma discectomy alters the expression of inflammatory cytokines in the degenerated lumbar discs of adult mini-pigs and may be capable of initiating a repair response by stimulating interleukin-8 (IL-8) production. Rhyu et al. [8] showed in an in vitro study on annular and nucleus pulposus (NP) cells that coblation has acute direct effects on proinflammatory mediator production by disc cells, influencing the expression of IL-8 and heat shock protein (HSP) 70. Other studies have demonstrated that the use of radiofrequency-based therapy initiates a cellular response by increasing the proliferation of both fibroblasts and epithelial cells and leads to accelerated wound closure [9,10].

Although clinical studies on coblation demonstrate promising results, the treatment effect mechanisms on which protocols can be optimized are still not well understood. The purpose of this study was to characterize the temporal and spatial pattern of healing after stab injury to the rabbit IVD, and to determine whether healing is enhanced by plasma-based bipolar radiofrequency treatment.

Materials and methods

Animals

The Institutional Animal Care and Use Committee at the University of California, San Francisco, approved all the outlined protocols. Twenty-three New Zealand white rabbits, weighing an average 4.2 Kg (range 2.9–4.9 Kg), were used in this study.

Stab injuries

Annular and nucleus stab injuries were performed under anesthesia using ketamine (10 mg/Kg, Ketaject; Phoenix Pharmaceuticals, St. Joseph, MO, USA) and xylazine (1.0 mg/Kg, Xyla-Jecta; Phoenix Pharmaceuticals, Inc.) as preanesthetic induction drugs. Buprenorphine (0.05 mg/Kg) and pancuronium (0.025 mg/Kg) were given preoperatively. After the animals were under deep sedation, they were intubated and given isoflurane (3%) with 2 LPM O_2. The animals were rested on a heating pad throughout the whole procedure to maintain constant body temperature. To avoid any wound infection, cefazolin (25 mg/Kg intravenously) was administered preoperatively, followed by enrofloxacin (5 mg/Kg) for 3 days postoperatively.

The rabbits were placed in a lateral prone position, and a posterolateral retroperitoneal approach was used to expose the anterior surfaces of three consecutive lumbar