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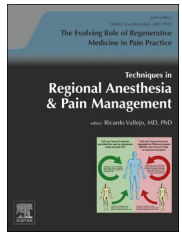

Treatment of annular disc tears and "leaky disc syndrome" with fibrin sealant

Kevin Pauza, MD[a,b,*], *Carrie Wright, BS*[a,b], *Adam Fairbourn, BS*[a,b]

[a]*Texas Spine and Joint Hospital, 1814 Roseland Blvd, Tyler, Texas 75701*
[b]*Manhattan Spine and Joint Institute, New York City, New York 10128*

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ABSTRACT

The surfaces of annulus fibrosus tears are known harbingers of inflammatory constituents within intervertebral discs, stimulating sensitized nocioceptors within those tears. Other current treatment options of internal disc disruption neglect to specifically address the surface of these tears. Therefore, this investigation answers the question: does non-autologous fibrin sealant applied to the surface of annulus fibrosus tears mechanically glue and seal annular tears? Regarding this query, results suggest nonautologous concentrated fibrin successfully seals annulus fibrosus tears with a "suture-like mechanical sealant," serving as a safe option for treating symptomatic or nonsymptomatic intervertebral disc tears. Sealing tears prevents pain-generating chemicals of the nucleus pulposus from leaking through annular tears. More specifically, fibrin sealant minimizes or eliminates extravasation of nucleus pulposus through tears and voids within the annulus fibrosus. Moreover, an investigation subjecting discs to an "internal pressure challenge" objectively affirms fibrin's ability to seal torn and degenerated discs against a pressure challenge. (1 psi = 6.89476 kPs (disc mean pressure pretreatment = 75.84 kPs; post-treatment = 179.3 kPs: ($n = 347$, $P < 0.001$). Therefore, sealing annular tears serves to minimize extravasation of nucleus pulposus through annular tears, thus potentially treating symptoms caused by internal disc disruption, "Leaky Disc Syndrome," and chemical radiculopathy. Additionally, sealing annular tears potentially allows adjunctive regenerative biologics such as mesenchymal precursor cells, platelet rich plasma, and growth factors to remain within discs, thus, potentially optimizing their efficacy. A prior in vivo investigation demonstrated the vast majority of mesenchymal stem cells leaked from animal intravertebral discs, and another demonstrated radiolabeled mesenchymal stem cells leaked from degenerated discs and were subsequently found within new exuberant osteophytes adjacent to the degenerated disc. Intra-annular nonautologous concentrated fibrin shares a benefit of other intradiscal biologics in that fibrin does not cause aberrant detrimental mechanical forces on adjacent discs, compared with surgical fusion and disc arthrodesis, which both cause aberrant, potentially damaging mechanical forces on adjacent segments. The mean number of morphologically abnormal lumbar intervertebral discs in this population with chronic low back pain was 3.21 discs.

*Corresponding author.
E-mail address: kevinpauza@gmail.com (K. Pauza).

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Introduction

Intra-annular fibrin treatment targets annulus fibrosus tears because the surfaces of these tears are known harbingers of inflammatory constituents within the intervertebral disc[1-5] stimulating nocioceptors within those tears.[2,6] All other current treatments of internal disc disruption (IDD) neglect to specifically treat these tears.[7] Sealing annulus fibrosus tears potentially serves to minimize chemical radiculopathy by minimizing extravasation of nucleus pulposus through annular tears, thus minimizing symptoms referred to as "Leaky Disc Syndrome" or IDD.[1,3,5]

All current surgical and nonsurgical treatments of IDD fail to address the disc's underlying pathology in two critical manners. First, they fail to correct the disc's leaking nucleus pulposus and associated inflammatory cytokines known to cause IDD symptoms.[3,7-10] Second, those treatment options for intervertebral discs all fail to address abnormal morphology of adjacent discs.[7-10] Likewise, surgical discectomy worsens disc morphology of the treated disc by disrupting its annulus fibrosus, leading to accelerated disc degeneration of the treated disc[11-13] and the adjacent disc.[12]

Surgical disc fusion, first performed in 1911,[14] and disc arthrodesis[15] meant to treat IDD, both subject adjacent discs to aberrant mechanical forces[16] causing accelerated degeneration of adjacent discs,[13] referred to as the "domino effect."[17-19]

This investigation revealed that in those subjects suffering from chronic low back pain, annulograms identified abnormal annulus fibrosis morphology with a mean of 3.21 discs, and with the mode being 3 discs (Table).

Surgical fusions and arthrodesis may lack reliable efficacy in that they fail to address "Leaky Disc Syndrome" associated with annular tears. More specifically, surgical fusions potentially allow persistent leakage of nucleus pulposus and other inflammatory components through lamellar tears of the annulus fibrosus of the fused intervertebral discs as well as adjacent discs. These inflammatory and autoimmune constituents may cause disc pain, and may potentially leak onto adjacent structures, affecting those tissues as well.[20-23] Therefore, fibrin application provides disc closure,[24] whereas conventional techniques, such as suture,[25] ligature,[25] glues,[25] or cautery, are ineffective or impractical.[26] Additionally, an in vivo investigation demonstrated decreased inflammatory constituents when compared with placebo controls in intervertebral discs treated with nonautologous fibrin.[24]

Historically, IDD symptoms were mistakenly attributed solely to pressure on the spinal nerve,[27-29] often referred to as a "pinched nerve." However investigations affirm that symptoms originate from heightened sensitivity of nocioceptors and chemical stimulation, with or without nerve root compression, and not nerve root compression alone, as historically believed.[20-23]

Background

The Food and Drug Administration approved this nonautologous fibrin sealant as an adjunct to standard surgical techniques (eg, suture, ligature, and cautery) to prevent leakage for the closure of colostomies, as an adjunct to hemostasis for general and cardiovascular surgery, and treatment of splenic injuries due to penetrating or blunt trauma to the abdomen.

This article describes a proprietary technique, for the intra-annular application of in situ catalyzed, biocompatible fibrin, made of specific ratios of concentrated nonautologous prothrombin and fibrinogen, to immediately mechanically seal annular tears, thus minimizing IDD and "leaky disc syndrome." The resultant fibrin serves as a bioadhesive glue, occupying voids and tears within the lamella of the torn annulus fibrosus. In comparison, other intradiscal biologic treatments that do not immediately form mechanically firm 3-dimensional matrices like fibrin that may leak through annular tears, whereas fibrin glue forms a 3-dimensional resorbable matrix sealing the disc's annular tears,[26] thus preventing leakage.

Sealing discs with fibrin may provide benefits in addition to treating the aforementioned disc symptomology. Specifically, sealing annular tears potentially allows adjunctive regenerative biologics such as MPCs, platelet-rich plasma, and growth factors to remain within discs, optimizing their efficacy, because research suggests cellular regenerative biologics might otherwise leak from torn intervertebral discs.[30]

Two studies demonstrate that the likelihood of MSCs remaining within torn intervertebral discs is low; demonstrating immediate profuse leakage of MSC.[30,31] One study introducing radiolabeled MSCs into artificially degenerated live animal discs demonstrating over 90% leakage from discs within 10 days.[30] Those radiolabeled MSCs were subsequently found within exuberant osseous overgrowth in the ring apophysis of the adjacent vertebral body.[30]

Table 1 – Intradiscal pressure values of normal and abnormal lumbar discs.

	Patients with LBP	Lumbar discs	Normal	Abnormal
	108	540	193	347
Mean Discs	–	5	1.79	3.21
% of discs	–	–	35.7	64.3
Mode	–	–	2	3
Mean pressure (preop, kPs)	–	–	158.6	75.84
Mean pressure (postop, kPs)	–	–	–	179.3
Mean Δ change	–	–	–	103.4

kPs, killopascals (1 psi = 6.895 kPs).

This first technique description uses annulograms to assess the integrity of the annulus fibrosus' integrity of all regional discs, and then subsequently treats all morphologically abnormal discs with nonautologous fibrin sealant. Sealed discs demonstrate increased resistance against pressure challenge (delta kPs = 103.4, $n = 347$, $P < 0.001$). Because computed tomography[32] and magnetic resonance imaging[33] identify anatomy, while lacking ability to discern disc symptomology, annulograms[32] are used immediately preceding fibrin sealant treatment. Annulograms assess dynamic contrast flow patterns through the annulus, and assess competency of lamella throughout the entire depth of the annulus fibrosus, and not just its inner margins. Additionally, annulograms affirm there is no vascular flow pattern before introducing fibrin through the same needle, which introduced radiopaque contrast. In comparison, provocation discography lacks the ability to routinely assess competency of the outer margins of the annulus fibrosus[34] because discography introduces radiopaque contrast to the disc's central nucleus pulposus only, which potentially precludes contrast flow through the disc's outer annular region. Additionally, investigations suggests provocation discography itself may cause iatrogenic intervertebral disc injury or accelerated disc degeneration.[35,36] In consideration of this adverse effect, this technique uses fibrin sealant to seal the needle hole, as well as annular tears.

Technique

After obtaining informed consent, prophylactic intravenous antibiotics, such as gentamicin are administered[37] before the patient is placed prone on the procedure table. Mild conscious sedation is obtained using short acting sedatives or analgesics such as midazolam or fentanyl, which is administered to the patient while monitoring their cardiopulmonary status. Using fluoroscopy, an ipsilateral oblique image is obtained of the targeted intervertebral disc so that the x-ray beam passes parallel to the ring apophysis and subchondral bone of the fibrocartilage endplate of the disc. With maximum radiographic "crispness" of the target disc, a curved tip Tuohy needle is directed toward the posterior annulus fibrosus of the intervertebral disc. Needle trajectory continues passing along the lateral surface of the superior articular process of that segmental level, allowing the needle to remain medial to the ipsilateral descending spinal nerves, until "purchase" is made into the posterior lateral aspect of the annulus fibrosus. Instead of targeting the nucleus pulposus, as is done in discography[38] and other disc access procedures, this needle tip is instead directed medially and posteriorly into the most posterior aspect of the annulus fibrosus. Anteroposterior and lateral images are obtained while the needle tip advances into the center, posterior aspect of the annulus fibrosus. Next, radiopaque contrast (0.75 mL gentamicin (40 mg/mL)) diluted into 30 mL of omnipaque 300 contrast medium[37] is introduced during dynamic fluoroscopy, allowing visualization of its flow pattern through the annulus fibrosus. Close scrutiny may reveal contrast flow into the vertebral canal and epidural space through noncompetent annulus fibrosus, and it is imperative to avoid vascular flow, to eliminate the likelihood of intravascular fibrin injection.

The needle remains in place, and if a morphologically abnormal disc is identified, the adjacent disc is tested in a similar manner. Each adjacent disc is sequentially tested until all discs are tested, or until a morphologically normal disc without annular tears is identified. The elicitation of symptoms during annulograms mattered not, because each annular tear was sealed and returned to normal morphological appearance, regardless of its symptoms produced while the annulus was tested.

The needle remained in place in all discs, including normal appearing discs. Following this diagnostic portion, highly concentrated, nonautologous prothrombin, fibrinogen, aprotinin, and calcium, were concurrently introduced to the internal surfaces of the tears of the annulus fibrosus using a multi-chambered device and the same curved needle. The iatrogenic needle hole was sealed in a similar manner while withdrawing the needle.

Therefore, upon completion, each disc's tears were glued and sealed, returning them to normal morphologic radiographic appearance. Fibrin volumes used depended upon extent of the annular tears and disc degeneration, and typically ranged from 1.5-6.0 cc/disc.

Additionally, radiopaque contrast was injected as an internal pressure challenge into the nucleus pulposus using digital manometry[39] at pretreatment and again at 5 minutes post-treatment. Intradiscal pressure was determined by observation of contrast first entering the nucleus pulposus, referred to as "opening pressure" was recorded.

Pressure values were obtained from all normal lumbar discs, and from all morphologically abnormal lumbar discs before their treatment and 5 minutes post-treatment with fibrin sealant.

After sterile dressings were placed, the patient is returned to the recovery room, before their discharge after 60 minutes.

Data

The mean number of morphologically abnormal lumbar intervertebral discs per patient was 3.21 discs; with a mode of 3 discs.

Intradiscal pressure referred to as "opening disc pressure" was obtained using digital pressure manomentry.[39]

Pressure values were obtained from all normal lumbar discs, and from all morphologically abnormal lumbar discs before their treatment and 5 minutes post-treatment with fibrin sealant.

Evaluation of 540 lumbar discs in 108 sequential patients over a 23 month period revealed 347 discs demonstrated abnormal annulus fibrosus morphology. The mean number of abnormal discs per patient.

Disc mean pressure pretreatment = 75.84 kPs; post-treatment = 179.3 kPs ($n = 347$, $P < 0.001$). Delta $P = 103.46$ kPs.

Conclusion

This investigation objectively demonstrates the following findings clinically relevant when treating patients with chronic low back pain caused by IDD:

(1) Concentrated nonautologous fibrin seals degenerated intervertebral discs against a pressure challenge. Pretreatment vs post-treatment intradiscal pressure increased 103.46 kPs. (disc mean pressure pretreatment = 75.84 kPs; post-treatment = 179.3 kPs ($n = 347$, $P < 0.001$).
(2) The mean number of abnormal discs per patient with chronic low back pain was 3.21 discs, and the mode was 3 discs.
(3) Therefore, sealing annular tears may minimize extravasation of nucleus pulposus, and may additionally serve to contain intradiscal biologics, which might otherwise leak from degenerated intervertebral discs.
(4) Treating less than 3 intervertebral discs may be suboptimal, recognizing that typically greater than 3 discs possess abnormal annular morphology.

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