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Position Paper

Regenerative Injection Therapy (RIT):

Effectiveness and Appropriate Usage

By

The Florida Academy of Pain Medicine (FAPM)

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POSITION PAPER FROM THE FLORIDA ACADEMY OF PAIN MEDICINE (FAPM)
ON REGENERATIVE INJECTION THERAPY (RIT)

DEFINITION OF RIT

Regenerative Injection Therapy (RIT) is an interventional technique for treatment of chronic pain due to connective tissue diathesis by induction of collagen chemomodulation through inflammatory, proliferative and regenerative/reparative responses mediated by multiple growth factors. ^(18, 25, 49, 50, 92, 93, 113, 114)

INTRODUCTION

The purpose of this positional paper is:

1. To inform/familiarize the members of FAPM and the medical community at large regarding the validity of an under-utilized, type-specific treatment for chronic musculoskeletal pain related to connective tissue pathology.
2. To outline common indications and conditions treated with RIT, as well as contraindications thereto.
3. To encourage the use of RIT in the treatment of appropriate painful pathology of the connective tissue.

METHODOLOGY

To determine the validity of RIT/prolotherapy, a position paper committee of interventional pain physicians was formed and undertook a comprehensive review of pertinent literature. The committee reviewed 78 specific articles and nine text books, as well as 51 relevant articles and chapters from other text books.

FINDINGS

From 1937 through 2000, more than forty authors reported case studies, retrospective, prospective and animal experiment studies that evaluated the results of treatment with RIT. The calculated number of patients reported in those studies exceeded 530,000. Improvement in terms of return to work and previous functional/occupational activities was reported in 48% to 82% of the patients. The resolution of pain symptomatology was evaluated differently in various studies and ranged from zero to 100%. Complications included 28 pneumothoraces, two requiring chest tubes, 24 allergic reactions, one grand mal seizure, and one aseptic meningitis.

The findings of the FAPM committee substantially contrast with the position of the Department of Health and Human Services (DHHS), Florida Workmen's Compensation, and Medicare guidelines. The committee recommends consideration of the use of RIT as a type-specific treatment for post-traumatic degenerative, overuse and painful conditions of the musculoskeletal system related to pathology of the connective tissue.

For decades, a small group of allopathic and osteopathic physicians has been practicing the methodology known as Regenerative Injection Therapy (RIT), also known as known in the past as prolotherapy. Pilot, retrospective, open face prospective, and double blind placebo controlled studies have clearly indicated RIT's effectiveness in the treatment of chronic musculoskeletal pain arising from post-traumatic and degenerative changes in connective tissue such as ligaments, tendons, fascia, and intervertebral discs. ^(4, 5, 8-10, 12, 14-17, 20-22, 26-28, 35-36, 38-69, 73-83, 88-99, 101-104, 106-111, 113-118, 120-122, 124-128, 133-135)

Clinical and experimental electron microscopic studies have proven that structurally the newly formed connective tissue had biomechanical properties similar to those of normal ligaments and tendons. ^(78, 94, 99, 110)

Preliminary results of clinical prospective trials for chemonucleo-annuloplasty with proliferation-causing substances show significant promise. ^(35, 36, 81, 97)

The literature dealing with RIT has been evaluated. This information, in association with extensive clinical experience has found RIT to be an effective therapy for a number of chronic pain conditions. This position paper reviews the clinical and pathophysiological aspects of RIT. The Florida Academy of Pain Medicine endorses RIT when utilized appropriately for the treatment of specific chronic pain entities.

I. RIT MECHANISM OF ACTION

The RIT mechanism of action is complex and multifaceted. Six identified components include:

- 1) The mechanical transection of cells and matrix induced by the needle, causes cellular damage, stimulating an inflammatory cascade. ^(8, 18-20, 93, 113, 114, 118, 119, 132)
- 2) Compression of cells by the extracellular volume of the injected solution stimulates intracellular growth factors. ^(84-86, 93, 113)
- 3) Chemomodulation of collagen through inflammatory proliferative, regenerative/reparative responses induced by the chemical properties of the proliferants and mediated by cytokines and multiple growth factors. ^(7, 18, 24, 45, 49-53, 84-86, 93, 113)
- 4) Chemoneuromodulation of peripheral nociceptors and antidromic, orthodromic, sympathetic and axon reflex transmissions. ^(49, 57-64)
- 5) Modulation of local hemodynamics with changes in intraosseous pressure leading to the reduction of pain. Empirical observations suggest that a dextrose/lidocaine combination has a much more prolonged action than lidocaine alone. ^(57-64, 123, 129, 138)
- 6) A temporary repetitive stabilization of the painful hypermobile joints, induced by the inflammatory response to the proliferants, provides a better environment for regeneration and repair of affected ligaments and tendons. ^(38, 39, 49-55, 120, 121, 124, 127)

II. PUTATIVE PAIN GENERATING STRUCTURES ADDRESSED BY RIT

(1-45, 47-69, 71, 73-86, 89-93, 98-104, 106-111, 113-122, 124-128)

- 1) Ligaments: Intra-articular, periarticular, capsular
- 2) Tendons
- 3) Fascia
- 4) Entesis: the zone of insertion of ligament, tendon or articular capsule to bone
- 5) Intervertebral discs. Note: outer layers of the annulus represent a typical entesis.

III. TISSUE PATHOLOGY APPROPRIATELY TREATED WITH RIT

- 1) Sprain: Ligamentous injury at the fibro-osseous junction or intersubstance disruption secondary to sudden or severe twisting of a joint with stretching or tearing of ligaments. (24, 71, 86, 100)
- 2) Strain: Muscle/tendon injury at the fibromuscular or fibro-osseous interface. When concerned with peripheral muscles and tendons, sprains and strains are identified as separate injuries and in three stage gradations: first, second and third degree sprain and similarly for strain. No consensus exists among authors, and the definitions are quite vague, regarding vertebral and paravertebral ligaments and tendons. (24, 71, 86, 100)
- 3) Enthesopathy: A painful degenerative pathological process that results in deposition of poorly organized tissue, degeneration and tendinosis at the fibro-osseous interface and transition towards loss of function. (18, 24, 71, 86, 93, 101)
- 4) Tendinosis/Ligamentosis: A focal area of degenerative changes due to failure of cell matrix adaptation to excessive load and tissue hypoxia with a strong tendency toward chronic pain and dysfunction. (71, 80, 84-86, 93, 112, 114, 119)
- 5) Pathologic Ligament Laxity: a post-traumatic or congenital condition leading to painful hypermobility of the axial and peripheral joints. (7, 8, 38-43, 47-54)

IV. INDICATIONS FOR RIT

(1-45, 47-69, 71, 73-86, 89-93, 98-104, 106-111, 113-122, 124-128))

1. Chronic pain from ligaments or tendons secondary to sprains or strains.
2. Pain from overuse or occupational conditions known as "Repetitive Motion Disorders," i.e., neck and wrist pain in typists and computer operators, "tennis" and "golfers" elbows and chronic supraspinatus tendinosis.
3. Chronic postural pain of the cervical, thoracic, lumbar and lumbosacral regions.
4. Painful recurrent somatic dysfunctions secondary to ligament laxity that improves temporarily with manipulation. Painful hypermobility and subluxation at given peripheral or spinal articulation(s) or mobile segment(s) accompanied by a restricted range of motion at reciprocal segment(s).
5. Thoracic and lumbar vertebral compression fractures with a wedge deformity that exert additional stress on the posterior ligamento-tendinous complex.
6. Recurrent painful subluxations of ribs at the costotransverse, costovertebral and/or costosternal articulations.
7. Osteoarthritis of axial and peripheral joints, spondylosis, spondylolysis and spondylolisthesis
8. Painful cervical, thoracic, lumbar, lumbosacral and sacroiliac instability secondary to ligament laxity.
9. Intolerance to NSAIDs, steroids or opiates. RIT may be the treatment of choice if the patient fails to improve after physical therapy, chiropractic or osteopathic manipulations, steroid injections or radiofrequency denervation, or surgical interventions in the aforementioned conditions, or if such modalities are contraindicated.

V. SYNDROMES AND DIAGNOSTIC ENTITIES,
CAUSED BY LIGAMENT AND TENDON PATHOLOGY,
THAT HAVE BEEN SUCCESSFULLY TREATED WITH RIT

(4, 5, 8-22, 26-32, 34-70, 74-85, 87-103, 105-115, 119-121, 123-127, 131-134)

- | | |
|---|---|
| <ol style="list-style-type: none"> 1) Cervicocranial Syndrome
(cervicogenic headaches, secondary to ligament sprain and laxity, atlanto-axial and atlanto-occipital joint sprains, mid cervical zygoapophyseal sprains) 2) Temporomandibular Pain and Muscle Dysfunction Syndrome 3) Barre-Lieou Syndrome 4) Torticollis 5) Cervical segmental dysfunctions 6) Cervicobrachial Syndrome
(shoulder/neck pain) 7) Hyperextension/Hyperflexion injury Syndromes 8) Cervical, Thoracic and Lumbar Zygoapophyseal Syndromes 9) Cervical, Thoracic and Lumbar Sprain/Strain Syndrome 10) Costo-transverse joint pain 11) Costovertebral arthrosis/dysfunction 12) Slipping rib syndrome 13) Sternoclavicular arthrosis and repetitive sprain 14) Thoracic segmental dysfunction 15) Tietze's Syndrome/
costochondritis/chondrosis 16) Costosternal arthrosis 17) Xiphoidalgia syndrome 18) Acromioclavicular sprain/arthrosis | <ol style="list-style-type: none"> 19) Shoulder hand syndrome 20) Recurrent shoulder dislocations 21) Scapulothoracic crepitus 22) Iliocostalis Friction Syndrome 23) Iliac Crest Syndrome 24) Iliolumbar syndrome 25) Internal lumbar disc disruption 26) Interspinous pseudoarthrosis
(Baastrup's Disease) 27) Lumbar instability 28) Lumbar ligament sprain 29) Spondylolysis 30) Sacroiliac joint pain 31) Sacrococcygeal joint pain 32) Gluteal tendonosis 33) Trochanteric tendonosis 34) Myofascial Pain Syndromes 35) Ehlers-Danlos Syndrome 36) Osgood-Schlatter disease 37) Ankylosing Spondylitis
(Marie-Strumpell disease) 38) Failed Back Syndrome 39) Fibromyalgia Syndrome 40) Foot and/or ankle: <ul style="list-style-type: none"> • Sinus Tarsi Syndrome • Metatarsalgia • Chronic Ankle Sprain • Instability • Laxity of ligaments |
|---|---|

VI. CONTRAINDICATIONS TO RIT

1. Allergy to anesthetic or proliferant solutions or their ingredients such as dextrose, sodium morrhuate or phenol.
2. Acute non-reduced subluxations or dislocations.
3. Acute arthritis (septic or post-traumatic with hemarthrosis)
4. Acute bursitis or tendinitis
5. Capsular pattern shoulder and hip designating acute arthritis accompanied by tendinitis.
6. Acute gout or rheumatoid arthritis
7. Recent onset of a progressive neurologic deficit including but not limited to (severe intractable cephalgia, unilaterally dilated pupil, bladder dysfunction, bowel incontinence, etc).
8. Requests for a large quantity of sedation and/or narcotics before and after treatment.
9. Paraspinal neoplastic lesions involving the musculature and osseous structures.
10. Severe exacerbation of pain or lack of improvement after local anesthetic blocks.
11. Relative contraindications: central spinal canal, lateral recess and neural foraminal stenosis.

VII. COMMONLY UTILIZED SOLUTIONS

The most common solutions are dextrose based. Dilutions can be made with local anesthetic, for example, 1 ml of 50% dextrose mixed with 3 ml of 1% lidocaine. A gradual progression to 25% Dextrose solution has also been utilized. ^(27, 50, 93, 113, 114)

For intra-articular injection of the knee, 25% dextrose solution was utilized for decades. ⁽⁵⁰⁾ Recently, a 10% Dextrose solution has been investigated and also proven to be effective. ⁽¹¹⁵⁾

5% sodium morrhuate is a mixture of sodium salts of saturated and unsaturated fatty acids of cod liver oil and 2% benzyl alcohol. Note that the benzyl alcohol chemically is very similar to phenol and acts as a local anesthetic and preservative. ^(8, 50, 93, 101, 124)

Dextrose phenol glycerine solution consists of 25% dextrose, 2.5% phenol and 25% glycerine and is referred to as DPG or P2G. In all referenced studies, it was diluted with a local anesthetic of the practitioner's choice prior to injection. Dilution reported ratios are 1:1, 1:2 and 2:3. ^(5, 20-22, 26, 28, 50, 78-80, 108-110)

6% phenol in glycerine solution was utilized at donor harvest sites of the iliac crests for neurolytic and proliferative responses. ^(95, 135)

Other solutions utilized include pumice suspension, tetracycline, a mixture of chondroitin sulfate, glucosamine sulfate and dextrose. ^(14, 36, 37, 42-44, 50, 81)

VIII. CONCLUSIONS

(1-138)

- 1) RIT (known in the past as Prolotherapy) is a valuable method of treatment for correctly diagnosed chronic painful conditions of the locomotive systems.
- 2) Thorough familiarity of the physician with normal, pathologic, cross-sectional and clinical anatomy, as well as anatomical variations and functions are necessary to utilize this technique appropriately.
- 3) Current literature supports manipulation under local joint anesthesia and a series of local anesthetic blocks for diagnosis of somatic pain.
- 4) Use of RIT in an ambulatory setting is an acceptable standard of care in the community.
- 5) Current literature suggests that NSAIDs and steroid preparations have limited utility in chronic painful overuse conditions and in degenerative painful conditions of ligaments and tendons. However, they are occasionally helpful to curb a significant inflammatory reaction to proliferants. Microinterventional regenerative techniques and proper rehabilitation up to six months or a year supported with mild opioid analgesics may be more appropriate.

IX. SUMMARY

RIT is a safe and effective treatment modality that is very useful in a significant number of pain syndromes arising from ligament and tendon diathesis, as well as other clearly delineated pain problems.

Physicians who use RIT must be knowledgeable in clinical anatomy and function and should be properly trained in this technique via a combination of seminars/workshops, apprenticeships or visiting fellowships in order to safely and effectively utilize this treatment. The Florida Academy of Pain Medicine endorses RIT when administered appropriately for the treatment of specific chronic pain entities.

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