Prolotherapy for Lumbar Segmental Instability Associated with Degenerative Disc Disease

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ABSTRACT

Prolotherapy is an injection-based therapy that may be used in the management of chronic low back pain. In principle, injection solutions are formulated to produce an inflammatory response, which in turn promotes ligamentous and tendinous regeneration.

This case study series offers some ideas as to how Prolotherapy might be advantageous in the management of discogenic low back pain through improving vertebral segmental stability.

When the disc is of normal height, the ligaments that hold the spine together remain at normal length. As the disc height decreases as in degenerative disc disease, the vertebrae move closer together. The resultant loss of spinal ligament tension may allow vertebral segmental instability, leading to chronic pain.

Materials & Methods: *The study analysed twenty-one male & female patients aged 35 to 73 years with chronic low back pain and MRI-confirmed low lumbar DDD (some with multi-level disease). They underwent 3 sets of fluoroscopically-guided Prolotherapy injections 1-3 weeks apart. Oswestry scores were analysed pre-Prolotherapy, at 3 months and at 1 year. All Oswestry scores were recorded on 14 patients, with the remainder only having pre and 1 year follow-up scores reported.*

Results: *Pre-Prolotherapy Oswestry scores ranged in all patients from 12 to 44. 12 patients reported ADL or functional improvement scores of 80% or greater. 3 patients reported ADL or functional improvement scores of 70% at 1 year follow up. 3 patients also reported complete resolution of LBP and 100% ADL improvement at one-year follow-up with one of these patients becoming symptom-free at 3 months with results maintained at one-year follow-up. On patients for whom 3-month follow-up data was available, there was typically further improvement on ADLs and pain reduction on one-year follow-up.*
3 patients reported no ADL or pain reduction benefit at all from the Prolotherapy with one of these patients actually reporting worse LBP and ADL scores at both 3 month and one-year post Prolotherapy.
An inverse pattern of reduced pain scores in relation to improved ADL function was noted.

Conclusions: *These findings are consistent with the conclusions of other studies, in that Prolotherapy, in conjunction with rehabilitation would appear to be an effective part of the management pathway for discogenic low back pain associated with degenerative disc disease of the lumbar spine.*

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KEYWORDS: degenerative disc disease, lower back pain, Prolotherapy, Regenerative medicine, spinal ligaments.

Introduction

Regenerative medical therapies have become popular in the past few years with the evolution of techniques such as stem cell therapy and platelet rich plasma but the original regenerative treatment continues to exhibit significant beneficial effects whilst being a demonstrably safe and cost-effective form of "Regenerative Medicine."

Prolotherapy injections, using hypertonic dextrose, have been used for over 80 years and are gaining recognition as having a place in the management of chronic lower back pain.[1]

When the disc is of normal height, the ligaments that connect each vertebra to the one above and below, remain of normal length. As the disc height decreases in degenerative disc disease, the vertebra approximate. As a result, like a rubber band that loses tension, the ligaments of the spine become lax. This may contribute to excessive vertebral translation and pain by shearing pain-sensitive structures. Lumbar degenerative disc disease (LDDD)-

caused spinal ligamentous laxity may also reduce proprioceptive feedback. Lax ligaments do not stabilize the segment as they did prior to the disc degeneration. This laxity may result in chronic pain in the discs, facet joints or other structures.[2,3]

Prolotherapy injections produce an inflammatory response, which can augment collagen fibre and ligament structure regeneration, resulting in tightening and strengthening of spinal ligaments, thereby reducing the incidence of discogenic low back pain by improving intersegmental stability.

Summary of Background Data

The concept of spinal ligamentous laxity pain generation was supported by Magnuson 1944, who theorized that as pains recur after operations when no disc is found, the stress and strains do not occur at the lower lumbar intervertebral discs but on the ligaments and joints of the posterior spinal canal.[4]

Newman 1952 noted in his surgical experience that at the time of disc operations the common findings are a torn or inefficient supraspinous ligament and an unstable vertebra.[5] The inference of spinal ligamentous laxity preceding disc injury was also recognized by Alpers in 1953.[6]

Lumbar spinal ligaments have variable strength and act via different lever arm lengths to contribute to spinal stability. As an example, as a consequence of the longer moment arm from the spinous process to the instantaneous axis of rotation, ligaments such as the interspinous and supraspinous ligaments are able to provide significant resistance to excessive flexion.[7]

Degenerative processes of the spine are a consequence of genetics and aging and occur to a varying degree. Disc space narrowing due to compression or herniations predisposes to laxity of intervertebral ligaments.[2]

Resultant changes in load transmission across the end plates and translation of the instantaneous axis of rotation further increase the degenerative processes at the adjacent structures.[8]

While date suggests that the presence of a degenerative disc is not diagnostic of back pain, the severity of spinal degeneration (extent and number of levels affected) does correlate with increased risk for symptoms.[9]

The literature presents conflicting evidence regarding the efficacy of Prolotherapy injections in reducing pain and disability in patients with chronic low back pain. Conclusions are confounded by clinical heterogeneity amongst studies and by the presence of co-interventions. There was no evidence that Prolotherapy injections alone were more effective than control injections alone. However, in the presence of co-interventions, Prolotherapy injections were more effective than control injections, more so when both injections and co-interventions were controlled concurrently.[10]

The RCT trial of Ongley et al. 1987 demonstrated that Prolotherapy was better than placebo for the management of chronic LBP. Those who question the validity of the study cite patient selection, differences in local anesthetic dose, and initial spinal manipulations (Prolotherapy group) vs sham manipulation in the placebo group.[11]

As in Ongley's study, patients reviewed in the study reported here had adjunctive physiotherapy or osteopathic treatment.

A study using bioengineered, computer generated, multilevel disc degeneration models implied a relationship between stress on structures such as ligaments, facets and pedicles and multi-level lumbar disc degeneration.[3]

This same study also concluded that the stresses and forces surrounding ligaments, facets, and pedicles at certain vertebral levels of the spine were generally lower in spines where the disc degeneration is not "contiguous" (at every level) ie there is a "skipped-level" disc degeneration, compared to cases were there is contiguous multilevel disc degeneration, even when the skipped level cases contained more degenerative discs. Such studies as this, validate the conceptual relationship of LDDD with that of spinal ligamentous laxity.

Lumbar DDD with loss of disc height and hydration may therefore slacken spinal intervertebral ligaments once held taut by "plump" healthy discs. This may contribute to excessive vertebral translation and consequently pain by shearing of structures where there is known nociceptive

sensory nerve supply as in the annulus or facet joints.[12] Studies such as Toyone et al. which links LDDD to hypermobility may further support the concept between ligamentous laxity and discogenic lower back pain.[13]

Also, mechanoreceptors within the supraspinous/interspinous ligaments and ligamentum flavum, facet joints, and interspinous ligament affect proprioception.[14]

Spinal ligamentous laxity secondary to LDDD may also adversely affect the potential for effective proprioceptive feedback. Prolotherapy injections produce an inflammatory response, supplementing the body's natural healing processes by tightening and strengthening of spinal ligamentous structures, thereby limiting excessive vertebral translation. Improved intersegmental stability may in turn inhibit aberrant nociception activity and improve lumbar segmental proprioceptive function.

Prolotherapy targets ligaments, which due to limited blood supply may not undergo a training effective of comparative magnitude to other soft tissues. By provoking a low-grade and controlled spinal ligamentous inflammatory response with consequent repair processes, Prolotherapy may improve motor unit stability more effectively than rehabilitation exercises performed in isolation.

Methods

This was a retrospective case series following 21 patients with MRI-confirmed lumbar disc degeneration. Their Oswestry Disability Index (ODI), and functional pain scores are shown before and after receiving level specific, fluoroscopically-guided lumbar Prolotherapy injections. All were identified as having refractory low back pain/or non-radicular leg pain. These fluoroscopically-guided lumbar Prolotherapy injections were performed as per the Blackberry Clinic Protocol. (*See Figure 1.*) This consisted of 3 sets of spinal ligamentous injections at 1-3 weeks apart. (*See Table 1.*)

The hyperosmolar solution used, P2G, is comprised of dextrose 25%, glycerol 25% and phenol 2%. The P2G is also known as Ongley's solution, and was formulated by Dr. Ongley in the 1960's. The solution was mixed with 1% lidocaine in equal parts (50/50) to a total volume of 10 ml.

Figure 1. Fluoroscopic x-ray guided Prolotherapy.

Table 1. Protocol for Prolotherapy in the UK.

Small volumes of a solution containing hyperosmolar dextrose or a solution called P2G (25% dextrose, 25% glycerol, and 2% phenol) are injected around ligamento-periosteal junctions, teno-osseous junctions, or into joints. P2G, also known as Ongley's solution, was started by Dr. Milne (Bud) Ongley in 1960s.[8] Hence, some orthopaedic physicians still refer to the use of proliferant to treat ligamentous laxity as "Bongling," This solution was mixed with 0.5% lidocaine in equal parts (50/50) to a total volume of 10 ml. A common proliferant injectate used in the UK is a 50/50 mixture of P2G and 1% lidocaine. A weaker solution that can be used is 50% dextrose diluted with 1% lidocaine to form a 12.5–25% dextrose solution.

Prolotherapy is usually performed on three occasions initially, with 1–3 weeks between each treatment. A further course of three treatments is used if the first course is subjectively or objectively helpful on a visual analogue scale (VAS) for pain and/or the Oswestry Disability Index (ODI) but if the improvement is incomplete.

Verbal or written consent is obtained. Then with the patient in the prone position, injection is made, under fluoroscopic X-ray guidance, into 13 sites around the L4/5 and L5/S1 intervertebral segments. In the UK, most practitioners use 5 ml P2G mixed with 5 ml 1% lidocaine or a solution of dextrose with lidocaine.

Frequently, the S1 spinous process is not visible or may exhibit a spina bifida occulta, so it is not routinely injected.

There is frequently a flare of pain for 1–2 days after the injection and patients are warned about this. They are asked not to take non-steroidal anti-inflammatory drugs (NSAIDs) for the duration of the course of treatment. Patients are usually advised to walk for 20–30 minutes per day for 2 weeks after the last injection. This is assumed to encourage functional orientation of newly augmented collagen fibres. Research shows that best results for back pain are when the course of injections is accompanied by active rehabilitation and advice on self-management.

Petrides S, Hudson M, et al. UK Protocols for Lumbar Prolotherapy. The revised Textbook of Musculoskeletal Medicine. OUP Oxford, 2015.

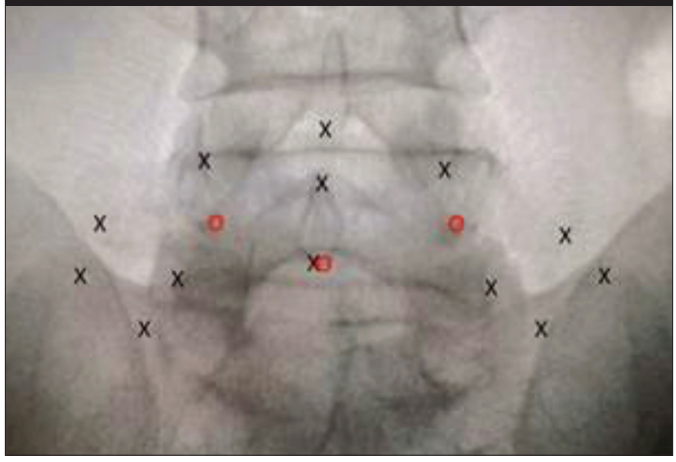
Verbal consent was obtained and recorded. Then, with the patient in a prone position, the injection was made with a strict aseptic technique and under fluoroscopic x-ray guidance, into 13 points around the L4-L5 & L5-S1 vertebral segments. The S1 spinous process may occasionally exhibit spina bifida occulta so is not routinely injected.

As illustrated in *Figure 2*, firstly 3 skin injection points were anaesthetized with 1% lidocaine using fluoroscopic guidance. Then injections were made into the ligamento-periosteal junctions at the origin and the insertion of the following ligaments:

1. the posterior sacroiliac ligaments
2. the iliolumbar ligaments
3. the facet joint capsules
4. the supraspinous and interspinous ligaments

Each of the 13 sites was infiltrated with 0.5-1ml of proliferant solution. Patients were warned that they may experience a flare of pain for 1-2 days post injection. They were asked not to take any non-steroidal anti-inflammatory medicine (NSAIDs) during the course of the treatment and for up to 2 weeks post injection. Patients were advised to walk 20-30 minutes per day for 2 weeks following the last injection. This is assumed to assist in the functional orientation of newly augmented collagen fibres since exercise provides physical stress to the healing tissue in order to promote organized remodeling through regeneration.

Figure 2. Red circles: skin entry sites. Black crosses: injection sites.



Oswestry Disability Index (ODI), Pain and Activity of Daily Living scores (ADL) were recorded pre-treatment, at 3 months and at 1 year post treatment via a mailed questionnaire. In 14 of the 21 patients studied, we were able to record results at all stages with the remainder having just pre and 1 year follow up scores recorded.

Patient ages ranged from 35-73 (mean age 51.4), and included 4 females, and 15 males of varied occupations and sporting participation. Pre treatment duration of LBP for 9 of the patients ranged from 18 months to 14 years with a mean of 8.2 years. Eight patients had pre treatment LBP for less than one year and from 1.5 to 10 months with a mean of 8.4 months. Duration of pre-treatment pain duration was not available for the remaining patients. The sex of 2 of the remaining patients was not recorded. All had lower lumbar segment DDD and some had multi-level disease.

Results

Pre-Prolotherapy ODI scores ranged in all patients from 12-44. Of a total of 21 patients, 18 patients (86%) experienced a 70% or greater improvement in pain and function at one year. Three patients reported complete resolution of LBP and 100% ADL improvement at one-year follow-up with one of these patients becoming symptom-free at 3 months with results maintained at one-year follow-up. 12 patients reported ODI and ADL improvements of 80% or greater. Three patients achieved Pain Score reduction and ADL improvements of 70% or better on one-year follow-up. Two patients reported no ADL/ODI pain reduction benefits at all from the Prolotherapy. One patient reported worse LBP and ADL/ODI scores at both 3 months and one-year follow-up. On patients for whom 3-month follow-up data was available, an improvement was typically followed by further improvement on ADL/ODI pain reduction on one-year follow-up. One patient, for whom lumbar fusion surgery was recommended, reported 90/90 ADL/ODI improvements on one-year follow-up. An inverse pattern of reduced pain scores in relation to improved ADL function was noted. (*See Table 2.*)

Table 2.

Patient No Physio Y/N Age/Sex/Occ	DDD Level Prolo Level	ODI Score Pre 3/12 1 year	Pain 1 yr f/u ADL 1 yr
1. 60617 Y 52F, Flight Attendant	D L4/L5 P L4/L5	28 No record 8	80% Decreased 80% Improved
2. 44835 50M, Music Teacher Yes +Osteopathy	D L4/5 P L4/5 (CE prior)	38 2 0	100 100
3. 53689 Y 48M Police	D L4-S1 PL5/S1	40 46 46	0 0
4. 63292 Yes 51M Office worker	DL3-5 PL4/5	30 6 2	85 85
5. 65690 Y+Pilates 51M-Occupation Unk *TLIF (fusion) recom	D L4-S1 P L4-S1	38 0 8	90 90
6. 55099 Yes 44M-IT	D L3-S1 P L4-S1	36 56 18	80 90
7. 27512 Yes+Osteo 52F -Secrete	D L3-S1 P L4-L5	40 No record 0	100 100
8. 66273 Yes 44M-Finance	D L2-4 P L3-5	34 20 4	80 80
9. 67363 Yes 45M-Occupation Unk	D L5-S1 P L5-S1-SIJ	44 No record 0	90 90
10. 67753 Y 36F-Retired Ballet Dancer	D L5-S1 P L5-S1	16 2 2	90 90
11. 53498 Y ?AgeM-Rower	D L5-S1 P L5-S1	16 2 2	90 90
12. 56599 Y 37M Per. trainer	D L5-S1 P L5-S1	20 12 14	100 75
13. 56952 Y 45M-Coach	D L5-S1 annular tear P L4-S1	12 0 0	100 100

Table continued on next column

Table 2. Continued.

Patient No Physio Y/N Age/Sex/Occ	DDD Level Prolo Level	ODI Score Pre 3/12 1 year	Pain 1 yr f/u ADL 1 yr
14. 58173 Y 39M ex Cyclist	D L5-S1 P L5-S1	20 No record 16	25 100
15. 57378 Y 73M-retired	D L4-L5 P L5-S1	18 28 26	0 0
16. 57661 Y+Osteo, 45F-hairdrsr	D L3-S1 P L3-L5	22 22 38	0 0
17. 60617 Y ?Age/Sex/Occ	D L4-L5 P L4-L5	26 No record 8	80 80
18. 52280 Y 52M-Occ Unk	D L4-L5 P L4-S1	4 10 ?? 12 ??	70 70
19. 53498 Y 35M-Rower	D L4-L5 P L4-L5	10 2 2	90 90
20. 61043 Y 73M-retired	D L4-L5 P L4-L5	16 0 2	100 90
21. 54804 ?Age/Sex/Occ	D L3-S1 P L4-L5	26 22 22	85 85

Discussion

In comparison to other soft tissues, ligaments have less vascularity. Once injured or degenerated, this lack of blood supply may delay healing. Prolotherapy may offer the stimulus for ligament regeneration. However, without a program of lumbar stabilization exercises, it is likely to be less effective in directing the healing tissues to become more organized, flexible and less prone to re-injury. Therefore, rehabilitative exercise is an essential component to achieve a maximum stabilization effect.[15]

The choice of therapeutic targets in the regime used in this study includes both spinal ligaments and facet joints. This takes into account a close linear association between facet joint (FJ) degeneration, increased FJ fluid index, and radiographic instability in the lower lumbar segments.[16]

Clinical assessment of the lumbar spine remains a vital part of the assessment of function. Recent biomedical engineering research in three-dimensional, non-linear modeling of the lumbar spine investigating the relationship between disc degeneration on ligament mechanics has demonstrated that lumbar lateral bending may be an important marker to detect the subtle changes associated with disc degeneration.[17]

Testing these findings fluoroscopically may add value to diagnostic work-up.

Fluoroscopy also has a role in assessing impact of treatment. One study reviewing results of fluoroscopic C-arm cervical spine Prolotherapy reported a statistically significant reduction of both cervical flexion and extension translation as well as a reduction in pain visual analogue scores.[18]

Fluoroscopic control was used in this series to provide documented consistency of treated anatomy. However, it is not known if image-guided Prolotherapy would provide any difference in outcome compared to Prolotherapy using anatomical landmarks, though it is presumed to be safer.

As in Ongley's study, patient's reviewed in this study had adjunctive physiotherapy or osteopathy, which is in keeping with specific adaptation to imposed demands principles,[19] in that Prolotherapy provides the stimulus and exercise provides physical stress to the healing tissue in order to promote organized remodeling throughout regeneration.

Strong and functional spinal ligamentous structures may help degenerated lumbar discs to better tolerate tensile and compressive loads.[20]

Conclusion

There are currently few treatment choices other than surgical fusion for intractable lumbar discogenic pain and instability. Prolotherapy may offer a minimally invasive, cost effective, and safe management option for these patients.

The findings in this study are in keeping with conclusions of other studies in that Prolotherapy, in conjunction with rehabilitation, would appear to be an effective intervention for the treatment of discogenic lower back pain associated with degenerative disc disease of the lumbar spine.[21,22]

Further research with a larger test group is warranted to confirm these findings as well as allowing for further case selection on the basis of clinical and radiological findings.

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