Manuelle Medizin 2023 · 61:40–43
https://doi.org/10.1007/s00337-022-00934-7
Accepted: 7 December 2022
Published online: 2 January 2023

Achieving effective long-term therapeutic results in the treatment of chronic pain of musculoskeletal origin: the place of regenerative medicine

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Abstract

The use of regenerative medicine to treat injuries and degenerative conditions is gradually replacing more traditional methods. Regenerative techniques include prolotherapy, platelet-rich plasma, and stem cell injection, though the variety of injectable blood products is increasing. These techniques can be used to successfully treat conditions like partial tendon and ligament tears, chronic low back and neck pain, osteoarthritis, and even localized neuropathic disorders. In many instances, surgery may be avoided or at the very least delayed. Regenerative techniques will likely take the place of corticosteroid injections, which have been shown to only offer temporary relief for many of the musculoskeletal conditions treated, and frequently worsen the condition when repeated. Because the body develops various biomechanical compensatory mechanisms to avoid pain and function better, other body parts function suboptimally and eventually develop pathologies as well. Therefore, the practitioner must perform a methodical clinical evaluation to assess the musculoskeletal system as comprehensively as possible. Then one can best address the individual pathologies using the various tools at hand. Regenerative medicine has shown much potential in achieving successful long-term results, preventing much unnecessary surgery, and reducing the need for analgesia.

Keywords
Prolotherapy · Platelet-rich plasma · Musculoskeletal system · Low back pain · Osteoarthritis

"Stem cell research can revolutionize medicine more than anything since antibiotics." Ronald Reagan, 2004
"The regenerative Medicine revolution is upon us. Like iron and steel to the industrial revolution, like the microchip to the tech revolution, stem cells will be the driving force of this next revolution." Cade Hildreth.

We are entering a new era of regenerative medicine. Our body is loaded with pharmacology to heal its own injuries and aging tissues; we just need to optimize and activate this healing potential. However, though research has shown regenerative medicine to be effective, many studies still emerge with equivocal long-term results. Though no studies have compared treatments that were more comprehensive than those that were less so, many regenerative interventionists would claim from clinical experience that long-term success is dependent on, first and foremost, treating the disorder systematically. Reasons for this will be elaborated on below.

The basis for a systematic treatment of musculoskeletal disorders is a thorough and systematic clinical evaluation. In this article, two very common clinical examples are discussed, where most commonly, only the most pathological structure is treated, leading to good but short-term results.

The temptation to immediately refer the patient to imaging is always there,

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though nothing can really replace a systematic clinical evaluation of the whole region. Because several pathologies can coexist, some of which may be asymptomatic, it is often challenging to ascertain which is the pain-generating structure. However, because structures interact and function symbiotically, it is important to address *the whole functional unit* in order to achieve satisfying long-term results. This is all the more so in chronic cases, in which the patient adopts various biomechanical compensating mechanisms.

It is critical to understand that tissue degeneration, wherever it may be in the body, develops as a result of a force acting on the whole area, whereby one of the structures succumbs first. For example, in a patient with a rotator cuff tear, the supraspinatus tendon will usually be the first to succumb. However, forces applied to the supraspinatus eventually affect the neighboring structures as well. Partial [1] and full-thickness tears [2] have a 40% and 38% chance of progressing, respectively. Subluxation of the long head of the biceps tendon leads to an increased chance of subscapularis tendon tearing [3]. If the aim is to prevent spreading of the tear, then one must aim to stabilize or strengthen the whole region under duress.

The second example is the patient with spinal stenosis. These patients, who invariably have limited spinal movement, will develop "adjacent segment degeneration" in the regions below, namely the sacroiliac joints and ligaments [4], which are not as efficient in shock-absorbing as healthy structures. The joints themselves are more prone to wear and tear. The hip joints also bear the brunt of the dysfunctional lumbosacral complex and are more vulnerable to developing osteoarthritis [5, 6]. Sacroiliac and gluteal function are intimately related. All of the above-mentioned structures function symbiotically. Consequently, dysfunction of any of these is likely to impair the function of the others. And conversely, when one of these structures is diagnosed as causing pain, treatment should ideally address the whole functional unit. Treatment of only the pain-generating structure will likely lead to good results but only in the short term.

It is impractical to inject the whole of the lumbo–sacroiliac–hip–gluteal complex. However, for example, in order to achieve good long-term therapeutic results in the treatment of sacroiliac pain, one can inject the lumbo-sacroiliac ligaments, preferably using regenerative injections; prescribe exercises to strengthen the gluteal muscles; address ergonomic issues; and consider shock-absorbing shoes and loss of weight in order to reduce impact on the joints, thereby hopefully limiting advancement of the osteoarthritis. At a later date, one may consider injecting other structures.

The percentage of acute cases of low back pain (LBP) becoming chronic is rising and has been cited to be 19.6% of the population between the ages of 20 and 59 [7]. According to one meta-analysis [8], the prevalence of chronic LBP in those above the age of 60 varies between 21 and 75%. The elderly population in particular suffers from multiple coexisting degenerative pathologies. Athletes often suffer from multiple injuries, leaving more than one structure decompensated. Given that, for example, lumbar imaging findings are not necessarily related to the clinical scenario [9–11] and that the specificity of the straight leg raising test [12–14] is low, the exact diagnosis of the cause of low back pain can be quite challenging. The clinician must combine many clinical tests to arrive at a clinical diagnosis, and then include imaging findings if they match the clinical picture. Patients with one pathology, whether symptomatic or not, will invariably compensate for their impairments by limping, bearing weight on the other limb, stooping forwards, using the opposite shoulder, walking with crutches, and so on, all of which will lead to additional neighboring pathologies. Several structures become potential pain generators. The ideal method of treating these patients is using regenerative methods in a methodical fashion.

Regenerative injection therapy uses the body's repair mechanisms to repair its own damaged tissue, be it torn or lax tendons and ligaments or degenerative cartilage. Prolotherapy is the simplest of regenerative therapies, in which a nonbiological injectate, usually hypertonic dextrose, is injected. Prolotherapy has been found to promote collagen formation by stimulating the recruitment of fibroblasts, leading to the formation of stronger and thicker tendons and ligaments [15–17]. Dextrose has been found to promote chondrocyte replication [18, 19]. Several clinical studies have demonstrated a benefit of dextrose injections for the treatment of mild osteoarthritis [20–23]. Platelet-rich plasma (PRP) injections also have an anabolic effect due to the rich supply of various growth factors within the platelet granules and have been used for the treatment of tendon and ligament injuries and osteoarthritis [24–29]. Mesenchymal stem cells harvested from adipose tissue have several advantages over those harvested from bone marrow [30]. That's right! Even our own fat can be used for regenerating our own damaged tissues. Moreover, PRP and stem cells are widely used for aesthetic purposes in reversing aging skin and improving hair growth.

All of these regenerative treatments are effective in the treatment of these conditions, though prolotherapy and PRP injections are the easiest to implement, especially the former. Prolotherapy and PRP have rarely been compared head-to-head. Prolotherapy is cheap and easy to implement. However, because PRP technology has advanced tremendously in the past few years, it has become a whole class of treatments in itself, each with the emphasis on a different aspect of its regenerative properties. These include enrichment of cytokines, concentrated growth factors, use of scaffolds, blood separators, addition of coagulation activators, use of Wharton jelly [31], combining treatments with injection of collagen or hyaluronic acid [32, 33], and the list goes on. Injection of stem cells can treat effectively even grades 3 and 4 of degenerative osteoarthritis of the knee [34].

In this new era, I truly believe that steroids will become history for the treatment of most musculoskeletal disorders. We can explore our body's healing potential and reverse much of the degeneration in our tissues while avoiding the injection of chemicals and catabolic steroids. Regenerative injection therapy is generally safe, with fewer adverse effects than the current state-of-the-art alternatives. Let us dive into this new era and take on this challenge by treating our patients thor-

oughly and safely, in order to maximize our long-term treatment efficacy.

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Conflict of interest. O. Wende declares that she has no competing interests.

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Zusammenfassung

Erzielen effektiver Langzeittherapieergebnisse in der Therapie chronischer Schmerzen muskuloskeletalen Ursprungs: der Bereich regenerativer Medizin

Der Einsatz regenerativer Medizin zur Behandlung von Verletzungen und degenerativen Erkrankungen ersetzt nach und nach traditionellere Methoden. Regenerative Techniken umfassen die Prolotherapie sowie die Injektion von plättchenreichem Plasma und Stammzellen, obwohl die Vielfalt an injizierbaren Blutprodukten zunimmt. Diese Techniken können zur erfolgreichen Behandlung von partiellen Sehnen- und Bänderrissen, chronischen Rücken- und Nackenschmerzen, Osteoarthritis und sogar lokalisierten neuropathischen Erkrankungen eingesetzt werden. In vielen Fällen lässt sich eine Operation vermeiden oder zumindest hinauszögern. Regenerative Techniken werden schließlich Kortikosteroidinjektionen ersetzen, von denen gezeigt wurde, dass sie bei vielen der behandelten muskuloskeletalen Erkrankungen nur eine vorübergehende Linderung bieten und den Zustand häufig verschlimmern, wenn sie wiederholt werden. Der Körper entwickelt verschiedene biomechanische Kompensationsmechanismen, um Schmerzen zu vermeiden und Funktionen aufrechtzuerhalten. Als Folge der Kompensation arbeiten andere Körperteile suboptimal und entwickeln schließlich auch Pathologien. Daher muss der Behandler eine methodische klinische Bewertung durchführen, um den Bewegungsapparat möglichst umfassend zu beurteilen. Dann lassen sich die einzelnen Pathologien am besten mit den verschiedenen zur Verfügung stehenden Werkzeugen angehen. Regenerative Medizin zeigt ein großes Potenzial, erfolgreiche Langzeitergebnisse zu erzielen, viele unnötige Operationen zu vermeiden und den Bedarf an Analgetika zu reduzieren.

Schlüsselwörter
Prolotherapie · Plättchenreiches Plasma · Bewegungssystem · Unterer Rückenschmerz · Arthrose

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