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Case Report

Case series of ultrasound-guided platelet-rich plasma injections for sacroiliac joint dysfunction

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Abstract.
BACKGROUND: Two-thirds of adults worldwide will experience low back pain at some point in their life. In the following case series, we present four patients with sacroiliac (SI) joint instability and severe chronic low back pain, which was refractory to other treatment modalities.
OBJECTIVE: We investigated the efficacy of platelet-rich plasma (PRP) injections, a novel orthobiologic therapy, for reducing SI joint pain, improving quality of life, and maintaining a clinical effect.
METHODS: Short-form McGill Pain Questionnaire (SFM), Numeric Rating Scale (NRS), and Oswestry Low Back Pain and Disability Index were used for evaluation of treatment at pretreatment, 12-months and 48-months after treatment.
RESULTS: At follow-up 12-months post-treatment, pooled data from all patients reported a marked improvement in joint stability, a statistically significant reduction in pain, and improvement in quality of life. The clinical benefits of PRP were still significant at 4-years post-treatment.
CONCLUSIONS: Platelet-rich plasma therapy exhibits clinical usefulness in both pain reduction and for functional improvement in patients with chronic SI joint pain. The improvement in joint stability and low back pain was maintained at 1- and 4-years post-treatment.

Keywords: Musculoskeletal and joint disorders, drugs and medicines, orthopaedics, back pain, occupational and environmental medicine, Ehlers-Danlos syndrome, ligament laxity, sports and exercise medicine, fibromyalgia, neuropathic pain, motor vehicle accident

1. Introduction

An increasing number of people suffer from chronic low back pain, a debilitating condition which not only reduces patients' quality of life, but is also a heavy socioeconomic burden worldwide [1,2]. Broadly, the differential diagnoses for low back pain include non-mechanical, and mechanical causes such as sacroiliac (SI) joint instability [3]. The SI joints are weight-bearing diarthrodial joints, normally stabilized by the strong iliosacral, iliolumbar, sacrotuberous, and sacrospinal ligaments which limit its range of motion. The correlation between increased SI joint movement and

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low back pain was first documented in pregnant women over a century ago [4]. More recent studies estimate the prevalence of SI joint dysfunction as a cause for low back pain at up to 22.5% [5].

The diagnosis of SI joint instability is made by a combination of positive patient history, provocative tests, imaging, and diagnostic injections. Characteristically, SI joint associated low back pain is exacerbated by prolonged immobility, is unilateral in distribution, and radiates down the posterior compartment of the thigh. Current treatments for SI joint instability are however inadequate, varying from conservative management, to the use of non-steroidal anti-inflammatories (NSAIDs), opioids, botulinum-toxin-A, corticosteroid injections, prolotherapy, radiofrequency denervation, and surgical stabilization [6–9]. In this case series, we present four patients who were successfully treated for SI joint instability and chronic low back pain using PRP injections.

2. Case reports

2.1. Case 1

A 45-year-old woman with a past medical history significant for Ehlers-Danlos syndrome, fibromyalgia and anterior L3-S1 spinal fusion presented with new onset left-sided low back pain following a motor vehicle accident, causing her to require assistance with activities of daily living. On initial assessment, her short-form McGill Pain Questionnaire (SFM) score was 34/45, with a Numerical Rating Scale for pain (NRS) of 7/10, and an Oswestry Low Back Pain and Disability score of 46/50. On examination, there was marked tenderness and spasm of the adjacent piriformis muscle upon anterior-posterior and vertical stressing of the left SI joint. X-rays were negative for fractures, but a subsequent MRI identified bilateral bony sclerosis in the SI joints. Consequently, she was diagnosed with Grade 3 left SI joint instability (Femoral shear test grading: 0 = no instability; 1 = mild laxity; 2 = moderate, with end-feel on stressing joint; 3 = marked, with no end-feel; 4 = severe requiring surgery). No benefit was achieved from previous cortisone and a series of sodium morrhuate and dextrose prolotherapy injections into the left SI joint at Hackett's Points B and C. Short-term pain relief using NSAIDs and Tramadol was also inadequate.

2.2. Case 2

A 67-year-old woman with a past medical history significant for posterior L4-S1 spinal fusion presented with chronic right-sided low back pain following a previous tennis-related injury. The pain radiated down the lateral thigh, and interfered with her ability to walk or sit for prolonged periods. On initial assessment, her SFM score was 14/45, with an NRS of 4/10, and an Oswestry Low Back Pain and Disability score of 21/50. On examination, there was no numbness or paraesthesia, but there was marked tenderness over the right SI joint, and trigger points within iliopsoas and quadratus lumborum. Subsequent MRI scanning revealed severe degenerative changes in the right SI joint. Consequently, she was diagnosed with Grade 3 SI joint instability. She trialed a series of sodium morrhuate and dextrose prolotherapy injections into the right SI joint, from which no clinical improvement was noted.

Table 1
Lumbar spinal movements

	Patient score	Normal
Flexion	90°	90°
Extension	12°	30°
Left lateral flexion	14°	30°
Right lateral flexion	18°	30°

2.3. Case 3

A 40-year-old multiparous woman presented with a 3-year history of dyspareunia progressing to severe chronic low back pain. The pain was burning in sensation, and left her nearly bedridden. On initial assessment, her SFM score was 36/45, with an NRS of 7/10, and an Oswestry Low Back Pain and Disability score of 34/50. On examination, she had full range of motion of lumbar flexion, but limited extension and lateral flexion (Table 1). The tenderness in both SI joints was further associated with neuropathic signs including brush allodynia, and pinprick hyperalgesia over the lower back. Neurological examinations were otherwise normal. Following further investigation, she was diagnosed with Grade 2 right SI joint instability. A multi-disciplinary treatment plan including physiotherapy and spinal manipulations was employed. Pharmacological therapy with Onabotulinum Toxin A injections into the piriformis, paraspinal muscles (and intradermal into the allodynic skin), bupivacaine, Rofecoxib, and Hydromorphone also provided temporary pain relief.

2.4. Case 4

A 48-year-old woman with a past medical history significant for mild scoliosis at the T3 level presented

with a 3-year history of chronic low back pain following a fall. Localized to the left SI joint with radiation down both groins and the left lateral thigh, the pain was of sufficient severity to limit sitting and standing tolerance to 15 minutes. On initial assessment, her SFM score was 23/45, with an NRS of 7/10, and an Oswestry Low Back Pain and Disability score of 36/50. On examination, left straight leg raise was limited to 75°, and a positive left-sided response was observed to other SI joint manoevres including the Patrick's, Gaenslen's, Gillet's , Yeomen's, and shear test. X-rays were negative for fractures, but subsequent CT and MRI scanning revealed Grade 1 anterolisthesis at L4-L5, spondylolysis at L5, as well as concentric disc bulges and facet osteoarthropathy at L3-L4, L4-L5, and L5-S1. Consequently, she was diagnosed with Grade 2+ left SI joint instability. She noticed some clinical benefit following physiotherapy, as well as a trial of sodium morrhuate and dextrose prolotherapy injections at Hackett's Points A, B, C, and interspinous ligaments. Temporary pain relief was provided with low dose Pregabalin (25 mg BD).

3. Methods

Signed informed consent was provided from each patient for involvment in this study. We diagnosed SI joint instability through a combination of positive patient history, a physical examination including provocative SI joint manoeuvres [10] (Table 2), and imaging studies. X-rays, CT, and MRI scans were necessary to exclude pathologies such as fractures or malignancy, and to identify other abnormalties suggestive of osteoarthritic changes, herniated nuclei pulposi, or ankylosing spondylitis.

In our study, all autologous PRP was prepared using the Harvest Technologies SmartPReP 2 Platelet Concentrate System according to manufacturer's instructions. Briefly, 60 mL of venous blood was drawn aseptically and mixed with 8 mL of acid citrate dextrose solution. This anti-coagulated blood was subsequently centrifuged for 14 minutes at 3200 RPM to separate plasma from blood cells and the platelet concentrate. The platelet poor portion was removed and the remaining platelets with buffy coat (WBCs) and RBCs was remixed resulting in 10 mL of PRP (with a platelet concentration 5–6x above baseline). This was subsequently injected (3 inch 22 g needles) with ultrasound-guidance (13-6 MHz linear array probe; 5-2 MHz curved probe for subject 1) (Fig. 1) and using prolotherapy technique (0.5 ml with each needle contact of the ligament-bone interface) at Hackett's Points A, B, and C (Fig. 2). Injections were given after local anesthetic (preservative-free buffered lidocaine) was administered to the overlying skin and underlying muscle-fascia for patient comfort. Other than a "fullness discomfort" lasting 10–15 minutes post-injection, no adverse reactions were reported. Each patient received two sessions of PRP treatment. Statistical analyses and comparison of relative patient pain scores pre- and post-treatment was carried out using one-way ANOVA followed by Dunnett's Multiple Comparison test $P < 0.05$ (Fig. 3).

4. Results

Follow-up data for patients was obtained at 1-year and 4-years post-treatment, with the primary efficacy endpoint for PRP therapy in SI joint instability evaluated by changes in low back pain. Patients did not seek any alternative therapy during the follow-up period. The pooled data from all patients demonstrated a clinically and statistically significant reduction in pain at 1-year post treatment, as evidenced by a 93%, 88%, and 75% reduction in the mean SFM ($P < 0.0001$), NRS ($P < 0.001$) and Oswestry Low Back Pain and Disability ($P < 0.0001$) scores respectively (Fig. 3). The clinical benefits of PRP were still significant at 4-years post-treatment. Critically, patients achieved an improvement in their quality of life, and returned to their pre-injury statuses.

5. Discussion

PRP is autologous blood plasma containing an enriched platelet concentration of approximately 1 million platelets per microlitre – five times the baseline level [11]. The exact mechanisms by which PRP promotes tissue repair are poorly understood, but are likely to involve platelet degranulation and release of growth factors [12–18] (Table 3).

Currently, PRP is most frequently used in musculoskeletal tendinous and ligamentous injuries, where natural healing capacity is limited by poor vascularity. Indeed, one *in vitro* study demonstrated that PRP accelerated healing in tendinopathies through VEGF-induced neovascularization [19]. PRP was also shown to enhance gene expression of type I and type III collagen in equine tendons [20]. Further evidence was

Table 2
Orthopedic tests for evaluating SI joint dysfunction

Test name	Position	Method	Positive signs
Compression	Supine	Exert a medial force bilaterally from the anterior superior iliac spine (ASIS)	Increased pressure sensation in the SI joints
Distraction	Supine	Press bilaterally downwards and laterally on the ASIS	Unilateral gluteal or posterior leg pain
FABER/Patrick's	Supine	Place the test leg into flexion, abduction, and external rotation with the ankle resting above the patella of the opposite extended leg. Depress the knee towards the horizontal.	Pain before the knee depresses to the level of the opposite straight leg
Fortin Finger	Standing	Point to the area of the pain	Pain is localized with one finger, the area is immediately inferomedial to the posterior superior iliac spine (PSIS), and identified consistently over the last 2 trials
Gaenslen's	Supine	Flex both legs with knees against the chest and lower the test leg into extension	SI joint pain
Gillet's	Standing	Stand on one leg whilst bringing the opposite knee up towards the chest	Movement of the SI joint on the side the knee is flexed in a superior direction
Goldthwait's	Supine	Perform a straight leg raise	Pain before movement occurs at the interspinous spaces
Piedallu's Sign	Sitting	Compare the heights of each PSIS	The lower PSIS elevates above the PSIS of the opposite side on forward flexion
Prone Knee Bending	Prone	Flex patient's knee so that the heel is brought to the gluteal muscles	Rotation of the ipsilateral ASIS before the knee reaches 90° flexion
Shear	Prone	Apply pressure in a rostral direction to the sacrum near the coccyx, with simultaneous counter pressure against the legs	SI joint pain
	Supine	Apply pressure through long axis of femur with thigh flexed, abducted and laterally rotated 45 degrees from midline	SI joint laxity
Straight Leg Raising	Supine	Flex the leg with knee fully extended	SI joint pain
Yeoman's	Prone	Flex the test knee to 90° and extend the same hip	SI joint pain

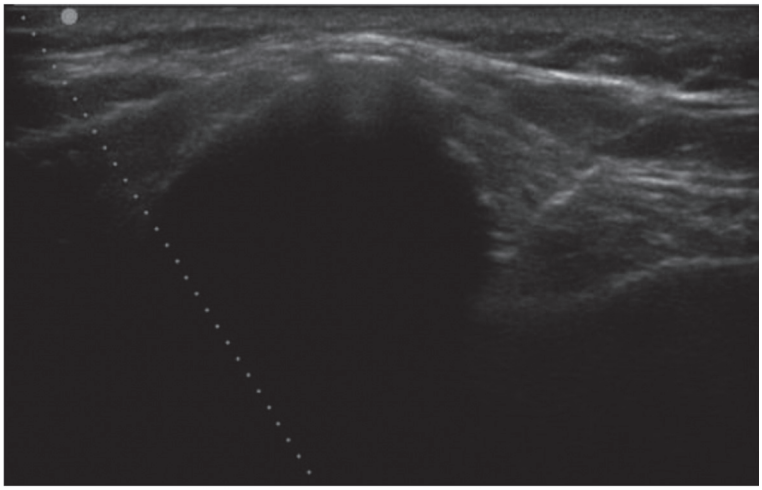

Fig. 1. PRP-injections performed under ultrasound guidance.

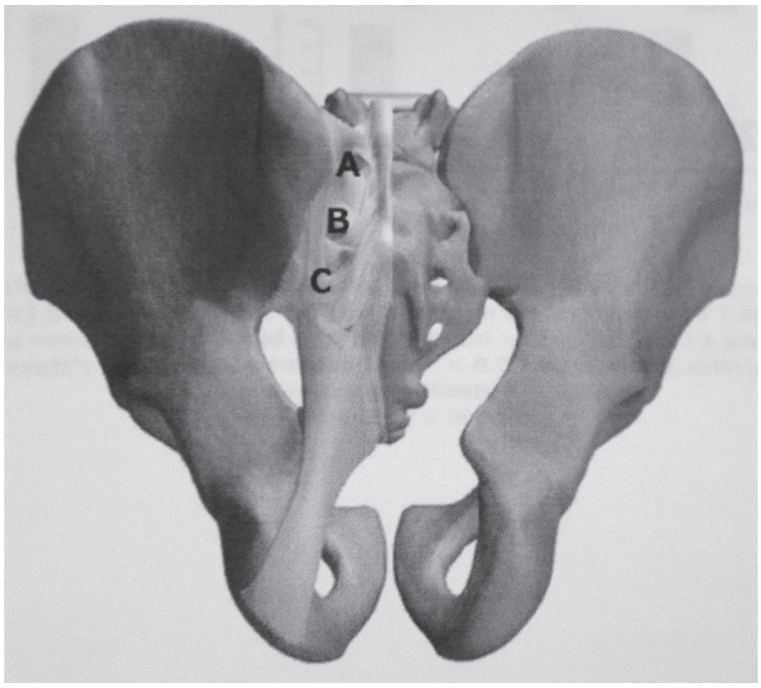

Fig. 2. PRP-injection sites. Injections were performed at Hackett's Point A, B (medial to the PSIS), and C (inferior to the PSIS).

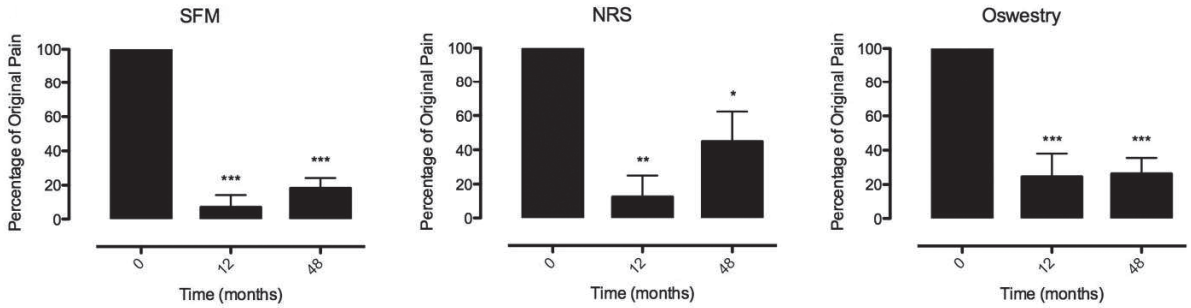

Fig. 3. Comparison of relative patient pain scores pre- and post-treatment. PRP therapy significantly improved patients (a) SFM, (b) NRS, and (c) Oswestry pain scores. Bars with 1 asterisk indicates a significant pain reduction compared to pre-treatment values based on a one-way ANOVA followed by Dunnett's Multiple Comparison test, $P < 0.05$. Bars with 2 asterisks indicate $P < 0.001$, and 3 asterisks indicate $P < 0.0001$.

provided by a rabbit patellar tendon defect model, whereby PRP therapy was significantly associated with IGF-1 overexpression and accelerated tendon healing as compared to controls [21]. Percutaneous PRP injectons into a transected Achilles tendon in a rat model also increased tendon callus strength and stiffness by 30% after one week [22]. Collectively, improved tendon mechanical properties in PRP treatment groups were observed [23]. Another clinical indication for PRP is osteoarthritis (OA) [24,25], since hyaluronic acid synthesis is stimulated by platelet released growth factors [26]. PRP injections have also been found to shorten recovery time after muscle strain injuries [27]. Thus, PRP appears beneficial in healing soft tissue injuries.

To our knowledge, this is the first study investigating the use of PRP therapy in SI joint related low back pain. PRP has previously been successfully used in the management of various soft tissue injuries. In the treatment of elbow epicondylar tendinosis, a single PRP injection resulted in a sustained and significant reduction in pain over time [28], and was subsequently proven to be superior to corticosteroid injections in a double-blinded randomized-

Table 3
Summary of growth factors in platelet-rich plasma (PRP)

Growth factor	Function	Reference
TGF-β	Pro-inflammatory Regulates collagen synthesis and collagenase secretion Induces deposition of bone matrix	[12]
PDGF	Facilitates production of other growth factors Stimulates chemotaxis of fibroblasts, macrophages, and stem cells Contributes to tissue remodeling	[13]
IGF-1	Promotes protein synthesis and proliferation of fibroblasts and myoblasts Enhances collagen and matrix synthesis	[14]
VEGF	Promotes angiogenesis and increases vessel permeability	[15]
FGF	Promotes growth and differentiation of chondrocytes and osteoblasts Contributes to production of granulation tissue	[16]
EGF	Regulates collagenase secretion	[17,18]

Abbreviations: TGF-β (Transforming growth factor-β); PDGF (Platelet-derived growth factor); IGF-1 (Insulin-like growth factor-1); VEGF (Vascular endothelial growth factor); FGF (fibroblast growth factor); EGF (epidermal growth factor).

control trial [29]. In a separate prospective double-blinded randomized-controlled study of 53 patients with complete rotator cuff tear, surgical repair with PRP treatment was associated with a greater reduction in pain and improvement in strength than surgery alone at 3-months post-treatment [30]. The use of PRP therapy in conjuction with open surgical repair for Achilles tendon rupture in athletes was also linked to an earlier return to baseline function [31]. More recently, studies demonstrated that PRP injections showed significantly more, as well as longer efficacy than hyaluronic acid injections in reducing pain and recovering articular function in patients with OA [32]. A FDA sanctioned study demonstrated effectiveness and safety for OA of the knee [33]. Conversely, other studies have reported no additional benefit of PRP over standard treatments for both OA [34] and tendinous injuries [35]. Potential reasons for the differing results may arise from small study sizes, differences in PRP preparation, and patient group selection. Thus, PRP appears to be broadly beneficial in the treatment of both tendinopathies and degenerative cartilaginous lesions.

Current guidelines for the management of confirmed SI joint dysfunction begins with physiotherapy and oral analgesics. If no significant pain relief is achieved within six weeks, a trial of intra-articular corticosteroid injections is usually offered. Alternative options including radiofrequency denervation offer limited success in reducing pain and improving SI joint stability [36]. Since SI joint instability is associated with osteoarthritic degenerative changes, as well as ligamentous and tendinous injuries, we anticipate that PRP treatment will improve SI joint stability and consequently, reduce low back pain.

In this case series, we observed that patients achieved a clinically and statistically significant reduction in low back pain at follow up 1-year and 4-years post-treatment. However, the theraputic benefit was noticably less at 4-years post-treatment when evaluated by the SFM and NRS scores. It is plausable that the difference in the NRS score is erroneous – not only have previous studies found the NRS score to have limited accuracy [37], but there was no loss of theraputic benefit between 1-year and 4-years post-treatment when evaluated by the more specific Oswestry Low Back Pain and Disability Index. Alternatively, the clinical benefits from PRP treatment may diminish over time [30,38].

There was also several limitations to our study. We diagnosed SI joint instability on the basis of positive patient history, provocative tests, and imaging. However, the diagnostic value of examination tests for SI joint pain is limited [39]. Whilst the use of the provocative SI joint manoeuvres in combination improves accuracy [40], a definitive diagnosis requires a 90% or greater reduction in pain following fluoroscopically guided intra-articular injections of local anesthetic [41]. Moreover, needle stimulus also has therapeutic effects [42]. Without appropriate blinding and controls, it is not possible to determine its contribution to the overall clinical benefits derived from PRP injections. Consequently, further studies are needed to assess the efficacy of PRP in treating SI joint instability and low back pain.

6. Conclusions/take home messages

– Sacroiliac joint dysfunction-instability is a cause of chronic low back pain.

– The theoretical basis for the use of platelet-rich plasma therapy in tissue repair involves growth factors which stimulate angiogenesis and collagen production.
– We demonstrated that the use of platelet-rich plasma therapy in the treatment of sacroiliac joint instability resulted in a clinically and statistically significant decrease in low back pain at 1- and 4-years post-treatment.
– Larger double-blinded randomized-controlled trials are needed to evaluate overall risks and benefits of platelet-rich plasma therapy in sacroiliac joint dysfunction.

Conflict of interest

The authors have no conflict of interest to report.

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