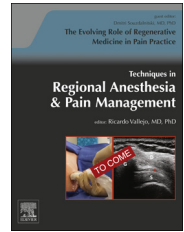


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# Regenerative medicine modalities for nondiscal spinal disorders

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## ABSTRACT

Regenerative medicine has demonstrated to have significant positive clinical outcomes. Its applications to multiple conditions, and potential for a healing result has caused some patients to seek out regenerative treatment options rather than considering surgical interventions once other conservative and interventional options have not been successful. In particular to the spine, much of the literature and attention has been on discogenic pain in the spine, followed by sacroiliac joint pain or syndrome. The applications of regenerative medicine in the peripheral joints, ligaments, tendons, and muscles can certainly be paralleled to many of the conditions and syndromes in the spine. Limited data and research are available; however, this is the cause for further research to be conducted.

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## Introduction

Regenerative medicine has certainly made its mark on the musculoskeletal medical world. Most often, our treatment protocols included conservative medication management, steroid injections, other noninvasive treatments similar to chiropractic care, acupuncture, physical and occupation therapy, as well as surgical interventions.<sup>1</sup> Over the past decades, platelet rich plasma (PRP) injections, bone marrow aspiration concentrate (BMAC) injection, and mesenchymal stem cell (MSC) preparations have come to the stage, and are asked for by patients before considering things like conventional injections and surgery.<sup>2</sup> As care providers, we need to be aware of this treatment option, as well as be proficient in knowing when it is applicable and when outcomes are going to be optimal.

## Background

Regenerative medicine has become popular treatment option for ligament, joint, and tendon disorders. Its effectiveness for

the peripheral joints, tendons, muscles, and ligaments has been well documented in some studies, whereas other has failed to demonstrate its efficacy.<sup>3,4</sup> Much of the data available is in case reports, case series, retrospective reviews, as well as in controlled clinical trials.<sup>3-5</sup> More recently, the use of regenerative medicine modalities for spinal disorders has been documented. There has been promise in the results for the use of degenerative disk disease. However, its applications to other pain syndromes in the spine have not been well demonstrated in controlled clinical studies.<sup>6</sup>

In theory, the process of tendon, ligament, and joint healing with the use of PRP and other regenerative techniques, should apply to common spine problems.<sup>7,8</sup> The same process of inflammation and pain generation that occurs in the peripheral regions of the body, also occur in the joints, ligaments, tendon, and muscles surrounding and supporting the spine whether it be the cervical, thoracic, lumbar, or sacral spinal regions.

Pain coming from the spine is one of the most common reasons for visiting the doctor. Its economic effect on the medical system is very cumbersome. With much of the

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criticism on the cost of conservative and interventional treatments, the effect on surgical interventions for both the medical system and patients is significantly damaging long term.<sup>9-11</sup> In turn, this limited improvement with surgical options, may be the reason for doctors and patients to pursue regenerative medicine options, and take a detour from the conventional algorithm of treatment.

### Mechanism of action

Regenerative medicine is thought to harness the healing factors from autologous blood, specifically the platelets, and at times using tissues that are concentrated with MSCs (from bone marrow and adipose tissues). The process is not fully understood, and much speculation exists regarding which factors are the most responsible for the phases of healing of injuries.<sup>12</sup>

In summary, PRP is thought to induce a healing cascade with the usage of platelets, specifically the alpha-granules, and dense granules. Concentrations of platelets in the serum can vary from individual to individual.<sup>13,14</sup> And further research is demonstrating that the platelet concentration for the intended tissue can be inhibitory or encourage healing. Then there is the debate regarding inclusion or exclusion of the buffy coat and white blood cell components.<sup>15</sup>

When using tissues with MSCs, the process is thought to introduce another element or level of healing; a cellular component of healing. These cells are thought to be responsible for tissue regeneration and developing into the surrounding environment of tissue they are placed into.<sup>16</sup>

Simply put, for healing and repair PRP is the cement whereas MSC are the bricks, and this allows for the masonry components of tissue regeneration and healing. The question that has yet to be answered is which one is better, and for which condition. This is the challenge we would be facing as specialist practicing regenerative medicine.

### Diagnosis and treatment options

Guidelines are available from different medical communities and societies, with little consensus among one another. Multiple vendors for PRP systems, and cellular products, have attempted to demonstrate that their approach is superior to others by doing platelet concentration measure and cell counts, postulating that this correlation would demonstrate healing and efficacy.<sup>17,18</sup>

In most cases, patients are told to avoid medications that may result in interruption of platelet functions before injection as well as postinjection. Postinjection recovery is usually minimal, and may require some pain medication to control.<sup>19</sup>

Before any injection, history and physical examination is paramount, to achieving correct diagnosis. Imaging is also very important. Diagnostic blocks before initiating a regenerative injection may be helpful as well. Once the appropriate pain generator is determined, blood work with platelet count may be helpful. This is often left to the practitioner. As Mishra et al<sup>14,15</sup> have demonstrated platelet counts vary from individual, and concentration system. Multiple factors need

to be considered when using regenerative techniques, and are the responsibility of the physician to maximize outcome.

The spine is often a location of pain, and much attention has been placed on the discogenic pain and regenerative interventions for them, followed by sacroiliac joint pain and syndrome.<sup>6,20,21</sup> However, the same principles in application to the disk and sacroiliac joint, along with the peripherals joints, ligaments, tendons, and muscles can be applied to the other conditions we see in the cervical, thoracic, lumbar, and sacral spines.<sup>21</sup> There is little research and data on these other conditions, and further cases series, and studies need to be done.

### Whiplash injury, cervical sprain, and lumbar spine sprain

The use of regenerative techniques in prolonged muscular pain, as in the case of whiplash injuries, myofascial pain, and muscle strain has limited literature available. However, studies have looked at the use of PRP and MSC injections for peripheral muscle repair and tendon injuries.<sup>22</sup> In the case of acute strain of the cervical, thoracic, and lumbar spine musculature typical conservative treatments are effective and curative in most cases.<sup>23</sup>

In more persistent and chronic cases, the use of treatments like PRP can be considered.<sup>24</sup> The literature that supports much of the peripheral joint injections for muscle and tendon strain can be applied in these cases as well.<sup>21,22</sup>

Furthermore, the application of trigger point injections to muscle pain in the spine has been used for decades. The debate regarding “wet” and “dry” needle has also lead some to believe that the actual needle trauma from the Trigger Point Injection induces bleeding around the muscle and trigger point, hence, inducing a regenerative event by blood products leaking out and around the site of pain.<sup>24</sup>

### Facet joint pain and syndromre

Facet pain is often the result of stress or degeneration on the small joints, which articulate the vertebral bodies posteriorly. They help with twisting, flexion, extension, and rotation. Facet generated pain is usually diagnosed with physical examination, imaging, followed by intra-articular joint injection with fluoroscopic or ultrasound guidance. In more persistent cases, a second injection or series of diagnostic blocks can be done to confirm the pain generator, which then may lead to a neurodestructive procedure for more long-term relief.<sup>25</sup>

In chronic cases, the application of PRP or MSC may be warranted. Limited data are available regarding the outcomes of this type of treatment; however, parallels from the literature can be made to help postulate an application in this region of the spine.

### Sacral fractures

In the same realm of using PRP for hip joint avascular necrosis and sclerotic bone, PRP and other regenerative injections can be used to help with healing, as well as the pain generated from these sacral regions.<sup>26</sup>

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