

## **EDITORIAL VIEW**

# **Chronic pain and regenerative medicine**

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### **ABSTRACT**

Chronic pains is becoming an epidemic in modern times but there are only a limited number of pain centers fully capable of addressing chronic pain issues. There are at least 667,000 individuals with chronic pains to one pain center in USA. There is a growing need for identifying etiological factors causing the pain rather than just treating the pain itself if applicable. Robinson and Singh has identified three approaches to address chronic pain management. The curative approach is the most simple. The palliative approach serves to assist the rehabilitation of the patient such as when pain interferes with functions by providing temporary pain relief. The release of substance P and CGRP (calcitonin gene-related peptide) can be affected by using a simple dextrose water solution injection (prolotherapy) on affected nerves in chronic pain syndromes. This technique forms part of the regenerative approaches which to many practitioners using this technique is simple and safe in contrast to pain medications whose side effect can be more detrimental than the original disease being treated. The other regenerative treatment used for chronic pain intervention is platelet rich plasma therapy. Regenerative injection therapies such as prolotherapy and platelet rich plasma might just be one solution that we are looking for in addressing chronic pain. As part of a team approach modality, these newer interventions may offer a pain cure and not just the treatment of pain itself.

**Key words:** Chronic pain; Regenerative injection therapy; Pain; Pain medication; Platelet rich plasma; Prolotherapy

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While it is true that we perceive pain from different perspectives based on our background and training, the patient who comes to us has only one objective in mind and that is to be relieved of his or her pain. Shatman in his editorial cited at least 100 million Americans suffering from chronic pain in 2010. For this number of patients, there are about 150 pain programs available, making it about 667,000 chronic pain sufferers attending a pain program.<sup>1</sup> These pain programs have varied treatment approaches and protocols. Speaking from the perspective of a physiatrist, I would like to share the view of Stanos et al, that there is a paradigm shift of treatment from mere analgesia, to one that is aimed to improve functionality.<sup>2</sup> With this in mind, the success of treatment of chronic pain is not merely easing the pain itself, but bringing back the very meaning of life itself to the patient. Haig and

Grabois, however, have recognized the frustration of each practitioner when dealing with chronic pain. Firstly, the cure or an intervention for such pain is not available when you need it. Secondly, the most effective treatments for chronic pain usually have little to do with anatomic diagnosis.<sup>3</sup> And so, the question is raised as to what should be done. Both authors<sup>3</sup> have suggested that there must be a painstaking effort to look for a cure first. And thus efforts to shift to pain management strategies be made only once pain cure is not appropriate. I find this approach very ideal in the sense that it provides logic as to how we should approach a patient with chronic pain. As physicians we are all aware that we have our own specialty of practice. As a physiatrist, I see a lot of low back and joint pains most of the time. Once a patient comes to me with pelvic and abdominal pain, I would not hesitate to

refer them to a gynecologist or a surgeon, as they are in the best position to evaluate such problems. Remember, most of the drugs that are available for pain treatment are only partially effective; and whether we should start opioids or non-opioid medications certainly will be a big challenge for us as physicians.

Robinson and Singh have classified three different approaches to chronic pain management. These are; curative/disease modifying, rehabilitative and palliative.<sup>4</sup> They found the curative approach to be the simplest among the three and it should be adopted if applicable.<sup>3</sup> The rehabilitative approach is preferred according to these authors when two conditions are available; when the cure is not applicable and when the ultimate goal is to make the patient more functional. Palliative approaches could act as an adjunct especially during the actual rehabilitation sessions when pain is interfering with function and activity.<sup>4</sup> A thorough physical examination notwithstanding, the advanced tools for recognizing sports injuries, repetitive and cumulative strain injuries and chronic pain syndromes affecting the musculoskeletal systems, including radiographic images, magnetic resonance imaging (MRI) and portability of musculoskeletal ultrasound,<sup>5</sup> much of what patient now complains about can easily be visualized and thus appropriately managed and treated.

Recently, it has been found out that the more common myofascial pain syndromes are a result of an overuse activities with motor end plate irritability and acetylcholine release with resultant sustained muscle contraction.<sup>6</sup> Further studies show the local release of pro-inflammatory substances like substance P and CGRP (calcitonin gene-related peptide) from injured sensory neurons in a process called neurogenic inflammation, which underlies hyperalgesia and allodynia.<sup>7</sup> Other chronic conditions show similar findings and could be a specific target in providing pain cure in patients whose pain remains unabated for months in spite of the medications.<sup>8</sup>

Regenerative medicine is beginning to be relevant in addressing chronic pains. With the expected side effects of prolonged non-steroidal anti-inflammatory medications, chronic steroid intake, and even with sustained opioid and non-opioid medications, regenerative injection therapies come with a new promise. Coupled with the portability of musculoskeletal ultrasound as a tool for making immediate visualization and thus diagnosis of common musculoskeletal conditions,<sup>5</sup>

the application of regenerative injection therapies makes it more convenient. However, with the paucity of consistent studies and limited randomized controlled trial studies pose some challenges in its application.

Two important regenerative injection techniques worth mentioning here include prolotherapy and platelet rich plasma therapy. Prolotherapy (Lyftogmed technique) makes use of buffered 5% dextrose water as an agent to proliferate the site of chronic pains, where it has been found to show proximal swelling of an entrapped nerve with impediment of both anterograde and orthograde flow of important substances inside the peripheral nerve,<sup>9</sup> thus causing pain. Further, its been hypothesized that dextrose water can influence the exchange of sodium and potassium through a receptor called TRV1 (transient receptor vollenoid 1).<sup>9</sup> A recent study by Maniquis-Smigel on chronic low back pain was published showing the effectiveness of 5% dextrose water.<sup>10</sup> Prolotherapy is effective in chronic osteoarthritis of the knee,<sup>11,13</sup> enthesopathy, tendinopathies and ligament injuries,<sup>5,12</sup> and carpometacarpal joint of the thumb.<sup>11,14</sup> Platelet-rich plasma (PRP) therapy is a treatment modality derived from the alpha granules of the platelets after a two-staged spinning method where platelet is concentrated to 3-6 times normal to extract different growth factors such as platelet derived growth factor (PDGF), insulin-like growth factor (IGF), epidermal growth factor (EGF), vascular endothelial growth factor (VEGF), transforming growth factor-beta (TGF-beta) and connective tissue growth factor.<sup>5,15</sup> PRP and its growth factors can stimulate healing, regeneration of damaged tissues, and graft integration into ligaments, tendons and muscles<sup>15,16</sup> and restore normal function of the peripheral nerves.<sup>17,18,19</sup> PRP is ideally considered for treatment 3-6 months after an injury and when more than one injections is needed, an interval of about 2 weeks to about 6 weeks is considered.<sup>15</sup> Recent studies provide varied results for different tissues and it could be due to different preparations and systems involved.<sup>20</sup> The advantage of using PRP, especially for sports injury, is its capability for early return to sports by about 2-3 weeks compared to athletes with no PRP.<sup>15</sup>

Knowledge of the latest interventions for chronic pains is very important. We cannot discount the importance of exercise and physical therapy as adjunct modalities for treatment. Behavioral and cognitive therapies play a role as well. Chronic pain affecting the joints, tendons and ligaments

that have been refractory to common treatment modalities may be treated with regenerative injection therapies.<sup>6</sup> The value of its effectiveness could not be discounted in spite of limited study protocols and consistent results. Let us always remember that where there is an identifiable cause of chronic pain, it is always good to address it first, if it is not possible treat the pain.<sup>3</sup> As the good book

says in Isaiah 40:30 and 31---"Even the youths shall faint and be weary, and the young men shall utterly fall: but they that wait upon the Lord shall renew (regenerate) their strength; they shall mount up with wings as eagles; they shall run, and not be weary; and they shall walk, and not faint." He shall be our hope and source of healing!

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