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NARRATIVE REVIEW PAIN MANAGEMENT

Platelet rich plasma therapy for carpal tunnel syndrome

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ABSTRACT

Carpal tunnel syndrome (CTS) is the most frequent peripheral nerve entrapment neuropathy, accounting for about 90% of cases. CTS arises because of the median nerve compression in the carpal tunnel on the wrist, as the median nerve passes through the tunnel from the forearm to the hand. The available evidence regarding therapy for CTS, reveals that splinting therapy, corticosteroid injection, and surgery are not 100% effective in curing CTS so there is a need to search for other alternative therapies.

One of the pain therapies currently being developed in the medicine sector is platelet rich plasma (PRP). PRP refers to platelet concentrations in plasma higher than normal platelets circulating in the body. PRP has been extensively utilized as new secure therapy in dentistry, bone surgery, ophthalmology, neurosurgery, and plastic surgery for three decades. PRP contains several growth factors that can enhance the process of wound healing, angiogenesis, and regeneration of axons.

Regarding the use of PRP therapy in CTS there is still a lot of debate and the benefits of these therapies have been still questioned. However, there are currently numerous studies on the utilization of PRP therapy in CTS. In vitro and in vivo studies show that PRP has neuroprotective, neurogenic, and neuroinflammatory modulators on nerves. Recent studies have shown satisfactory results from the administration of PRP therapy in CTS cases.

PRP is a promising alternative therapy for mild to moderate CTS cases, but it is not recommended for treatment of severe CTS cases. There are no studies that conduct long-term follow-up after the administration of PRP therapy, so there is no documentation related to the long-term impact of PRP therapy in CTS cases.

Keywords: platelet rich plasma; carpal tunnel syndrome; human; medicine

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1. INTRODUCTION

Carpal tunnel syndrome (CTS) is the most prevalent entrapment neuropathy for about 90% of all entrapment neuropathy cases.[1] This has been known as the major reason of chronic neuropathic pain at upper extremity.[2] CTS is one of the diseases that has been reported by the labor statistics agency in developed countries as a disease that is often found among industrial workers.[3] CTS occurs in consequence of compression of the median nerve in the carpal tunnel at wrist.[3]

Treatment for CTS varies from conventional therapy (medicines, night splints, steroid injections, and physical or physiotherapy) to surgery, namely median nerve. decompression.[4] The available evidence regarding

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Table I: Ultrasound-guided PRP infiltration characteristics for nerves[16]

	Median Nerve	Ulnar Nerve	Common Peroneal Nerve	
			Approach 1	Approach 2
Indication	Neuropathy due to stress such as CTS	Neuropathy due to stress such as UTS	Nerve lesions related with knee injuries	
Sufferer Position	Sit with arms flexed and supported by flat surface	Supine position	Pronation position	Lateral position on normal side
Extremity Position	Supination, palms pointing up	Pronation, with elbows slightly bent and propped by a tender superficies	Lower extremity extension	Knees are slightly bent and propped by a tender superficies
Infiltration or Injection Location	Wrist, near the area below the radius	At the back of the epicondylus medialis, into the tunnel of cubital	Behind the thigh, near fossa poplitea on the top of genu	Lateral part of the genu, near the head of peroneal
Spuit	Luer-Lok, 3 mL	Luer-Lok, 3 mL	Luer-Lok, 5 mL	Luer-Lok, 5 mL
Pin	23 G/25 mm	23 G/25 mm	21 G/50 mm	21 G/50 mm
Heading	Proximal-distal	Both	Proximal-distal	Proximal-distal
Intraneural Volume	2 mL	3 mL	3 mL	3 mL
Perineural Volume	4 mL	6 mL	6 mL	6 mL

therapy for CTS, reveals that splinting therapy, corticosteroid injections, and surgery is not 100% effective for curing CTS so it is necessary to look for other alternative therapies.[1]

One of pain therapies currently being developed in the medical field is Platelet Rich Plasma (PRP). PRP points to a concentration of platelets in plasma that is higher than the regular circulating platelets in the body.[5] PRP has been extensively utilized as new secure therapy in dentistry, orthopedic surgery, ophthalmology, neurosurgery, and plastic surgery for three decades.[5] PRP contains growth factors that can promote axon regeneration, angiogenesis, and wound healing.[6] Nowadays more evidence suggests that PRP has more benefits in axon regeneration and nerve repair in experimental animals or in vitro administration.[7] Several studies have shown that PRP can be used as a therapy in CTS. From several studies that have been conducted to assess the PRP efficacy as CTS therapy, different results have been obtained.[7] PRP as CTS therapy has been widely used in various countries, but there is still not enough empirical evidence to validate the use of this therapy and its role. PRP as CTS therapy is still remain unclear. [4]

2. PLATELET RICH PLASMA AS THERAPY

Platelet rich plasma (PRP) is an autologous plasma that has above average platelet concentration. It points to a concentration of platelets in plasma that is higher than reguler circulating platelets in body.[7] Recent studies have revealed the potential of PRP as a therapeutic modality. PRP can only be formulated from uncoagulated blood since platelets will be part of the clot in clotted blood. [4]

There are wide variations in PRP preparation process. PRP is obtained from blood samples taken from patients

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while getting treatment. Taking 30 cc of venous blood will produce 3-5 cc of PRP relying on the individual baseline platelet count, instrument, and procedure.[8] Blood collection is performed with the adjunct of anticoagulant as well as citrate dextrose A to avoid platelet activation before its utilization. Then particular 'table top cold centrifuge' device is used.[8] In general, the PRP manufacturing technique is divided into two, namely the PRP method and the buffy coat method. The costs associated with the preparation of PRP are much lower than those commercial PRP kits.[9]

The α-granules of platelets that have not been activated in PRP contain PGF that are non-functional because these factors have not been produced or interacted with tissues.[10] To initiate the emergence of growth factors, platelets must be switched on. Thrombin is the most potent platelet activating agent.[11] Growth factor release occurs gradually over 7 days.[12]

Accelerating the healing process is one of the functions of PRP by providing various types of cytokines and growth factors from the α-granules in the platelets themselves.[13] Inside the platelets, there are cytokines that can convert growth factor-β (TGF-β), insulin-like growth factor (IGF-I, IGF-II), platelet-derived growth factor (PDGF), epidermal growth factor, fibroblast growth factor (FGF), vascular endothelial growth factor (VEGF), and endothelial cell growth factor. These cytokines have the necessary tasks in cell proliferation, cell differentiation, chemotaxis, and angiogenesis.[13]

There are still no clear data on the quantity of PRP to achieve the maximum therapeutic effect.[14] Various studies have shown that a platelet count of 106/μL on PRP is the most effective number. This number increases four to five times the existing average and is expected to be adequate to give significant results in the use of PRP.[14,15]

In cases of neuropathy, PRP can be used as conservative therapy or as adjuvant therapy during surgery.[5] Conservative therapy is administered through an ultrasound-guided injection procedure such as by intraneural or perineural infiltration. PRP as adjuvant therapy during surgery can be administered through an endoscopic neurolysis procedure or through an open surgical neurolysis procedure.[16]

Initially the use of PRP therapy in CTS was still debated and the benefits of this therapy were still questionable. However, there have been many studies on PRP therapy in CTS. In vitro and in vivo studies have shown that PRP has neuroprotective, neurogenic, and neuroinflammatory modulatory effects on nerves.[16] Recent studies have shown satisfactory results from administering PRP therapy in CTS.[15] Clinically, it has been proven that PRP injection can rectify clinical symptoms and motor and sensory function through the repair of nerve muscle units.[16] In vitro and in vivo studies have shown the neurotrophic impact of PRP on peripheral nerves because PRP itself comprises divers autogeneic neurotrophic growth factors. PRP improves neuropathic pain through platelet-releasing factors and stem cells that initiate cascade of injury healing processes, followed by tissue remodeling, injury improvement, and axon regeneration.[3] Other studies have shown that in CTS patients, cells in the flexor retinaculum are physiologically impaired. This pathological thickening of flexor retinaculum can return to normal due to the effects of growth factors contained in PRP. PRP injection is proven to be safe because it is well tolerated and have no side effects, infections, or persistent pain complaints after administration.[4]

A prospective, clinical, randomized controlled, double-blind study conducted by Malahias et al. suggested that a sole dose of PRP injection which is guided by ultrasound showed a positive effect in patients with mild to moderate CTS compared with placebo.[9] PRP comprises divers autogeneic neurotrophic growth factors as well as fibroblast growth factor, epidermal growth factor, platelet-derived growth factor, and transforming growth factors.[16] In accordance with Allampallam et al., therapy with this growth factor can effect cells response in CTS patients' flexor retinaculum (FR-CTS) compared to individuals without CTS (control FR), the responses are as follows: 1) Higher mitogenic response than cells control, 2) Compared to control cells, there was elevated type III collagen stimulation output and degrade type I collagen stimulation formation in CTS cells, and 3) More alpha 2 (I) collagen production than alpha 1 (I) in CTS cells rather than control cells.[14] One of the journal reviews conducted by Loh et al. until December 2017, concluded that ultrasound-guided PRP injection is likely to have only short-term symptomatic improvement in mild to moderate CTS.[3] Nevertheless, the insufficiency of long-term follow-up in previous studies made it difficult to know if there was a recurrence or not.[3]

A systematic review conducted by Malahias et al. until March 21st 2018 stated that a number of growth factors are detached and switched on after PRP injection in patients with CTS.[9] This can promote median nerve regeneration and rectify blood supply to the nerve by providing protection to the "blood-nerve barriers". Therefore, PRP can prevent microischemia and compartment syndrome-like conditions that occur inside the carpal tunnel in CTS patients.[7] PRP also reduces intracarpal inflammation in the subsynovial connective tissue which has lately been considered as CTS main process.[9] Histological studies proved that perineural PRP injection can affect the production frequency of type I and III collagen fibers by returning to normal tissue transformation.[9] In this systematic review, it was also stated that the clinical outcome of CTS patients who

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received PRP therapy was better than the group of patients who received control therapy.[4] However, US and NCS yield in the PRP-treated group were not constantly better than control group, and controversy still exists regarding their effect on VAS and BCTQ values, US CSA, and NCS EMG scores.[10] PRP appears to be promising alternative therapy for mild to moderate CTS, but not recommended for advanced cases.[4] There are no studies that have conducted long-term follow-up after PRP therapy, so there is no documentation regarding the long-term effect of PRP therapy in CTS.[9]

3. SUMMARY

Carpal tunnel syndrome is the most prevalent case of entrapment neuropathy. Treatment of CTS is generally conservative therapy. Conservative therapy is mostly helpful in mild to moderate CTS but most studies suggest that this is only short-term effect. Therefore, a study was developed for the provision of other alternative therapies. Another alternative therapy for CTS that has been widely studied is Platelet Rich Plasma (PRP) therapy.

It has been shown that divers growth factors are detached and switched on after PRP injection in CTS patients. PRP can prevent microischemia and conditions such as compartment syndrome that occur inside the carpal tunnel in CTS patients. PRP also reduces intracarpal inflammation and affects the frequency of type I and III collagen fiber output by restoring normal tissue modifications. There are no studies that have conducted long-term follow-up after PRP therapy, so there is no documentation regarding the long-term impacts of PRP therapy in CTS.

4. Conflict of Interest

The authors declare no conflict of interest.

5. Authors contribution

All authors took part in the literature search, manuscript writing and editing.

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