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COMPARISON OF PLATELET-RICH PLASMA WITH CORTICOSTEROID INJECTIONS FOR PATIENTS WITH MILD TO MODERATE CARPAL TUNNEL SYNDROME: A SYSTEMATIC REVIEW AND META-ANALYSIS OF CURRENT EVIDENCE IN RANDOMIZED CONTROLLED TRIALS

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ABSTRACT

Carpal tunnel syndrome (CTS) accounts for over 90% of peripheral entrapment neuropathy cases. Platelet-rich plasma (PRP), has shown promise due to its anti-inflammatory effects and potential to support axonal repair and neuronal regeneration. The aim of this study is to evaluate the comparative therapeutic efficacy of PRP and corticosteroid injections in treating mild to severe CTS, using a three-month follow-up period.Methods: This meta-analysis followed the PRISMA framework, reviewing studies from 2017 to 2022 in PubMed and the Cochrane Library that compare PRP and corticosteroid injections for CTS. Primary outcome including Visual Analog Scale (VAS), Sensory Peak Latency (SPL), Distal Motor Latency (DML), and the Boston Carpal Tunnel Questionnaire Symptom Severity Scale (BCTQ-SSS). Results: Four studies remained after matches the screening phase. This meta-analysis includes 245 patients, including 123 receiving PRP and 122 corticosteroid injections. When looking at the VAS 1 and 3 month periods, FSS 3 months, SSS 3 months, DML 1 and 3 months, and SPL 3 months, there were statistically significant changes better outcomes towards PRP injection group compared to the control group. Conclusion: PRP injections provided better short- to mid-term relief and improved electrophysiological outcomes compared to corticosteroid injections in mild to moderate CTS cases.

Keywords: carpal tunnel syndrome; corticosteroid; injection; meta-analysis; platelet-rich plasma

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INTRODUCTION

Nearly all instances of peripheral entrapment neuropathy (PEN) were caused by carpal tunnel syndrome (CTS).(Ghasemi-rad, 2014) Because splinting, injections of corticosteroids, and surgery are not always beneficial, it is important to investigate alternative therapies for carpal tunnel syndrome.(O'Connor et al., 2003; Raeissadat et al., 2014) Thenar eminence flattening, motor dysfunction with poor pinching or gripping, and persistent numbness and discomfort are some of the symptoms that may prompt patients to seek surgery.(Zhang et al., 2015) Evidence suggests that non-operative conservative therapies, including rest, changes to physical behavior, splinting, activities to enhance nerve gliding, manual therapy methods, anti-inflammatory drugs, and many CTS patients experience self-limiting symptoms.(Mohamed et al., 2016)

For this condition, local steroid injection is advised as a therapy option. The majority of recommendations advise trying local steroid injection or splinting before considering surgery, and numerous studies have demonstrated the efficacy of local steroid injections in symptom

alleviation, at least in the short term. Since there is substantial evidence for the benefits of steroid injections only in the short term, the function of steroids in the long term treatment of CTS is still debatable (Huisstede et al., 2014; Keith et al., 2010)

On the other hand, platelet-rich plasma (PRP), a biological result of concentrated platelets, includes many growth factors, has an anti-inflammatory and regenerating effect, and thus has a favorable influence on neural regeneration and axon repair.(Eltabl et al., 2020) While corticosteroid injections are often used to relieve CTS symptoms, their benefits tend to be short-term, and long-term efficacy remains uncertain. Platelet-rich plasma (PRP) has gained attention as an alternative due to its regenerative and anti-inflammatory properties, which could provide longer-lasting relief and functional improvements. This study aims to evaluate the effectiveness of PRP versus corticosteroid injections in treating mild to severe CTS over a three-month period to draw a conclusions.

METHOD

Search Strategy

In compliance with the PRISMA principles, a systematic review was carried out (Figure 1).(Liberati et al., 2009) After scouring the academic literature from 2017 to 2022, we were able to locate an English-language, full-length research that compared the effects of platelet-rich plasma (PRP) injection with those of corticosteroid injection in cases with mild to severe carpal tunnel syndrome. We searched PubMed, Google Scholar, and the Cochrane Library. For mild to severe carpal tunnel syndrome, this meta-analysis and comprehensive review focuses on injectable platelet-rich plasma (PRP) and corticosteroid injections. Outcome Measure, Platelet-rich Plasma Injection, Corticosteroid Injection, Mild-moderate Carpal Tunnel Syndrome, and the MeSH rule were all used in the search that was discovered.

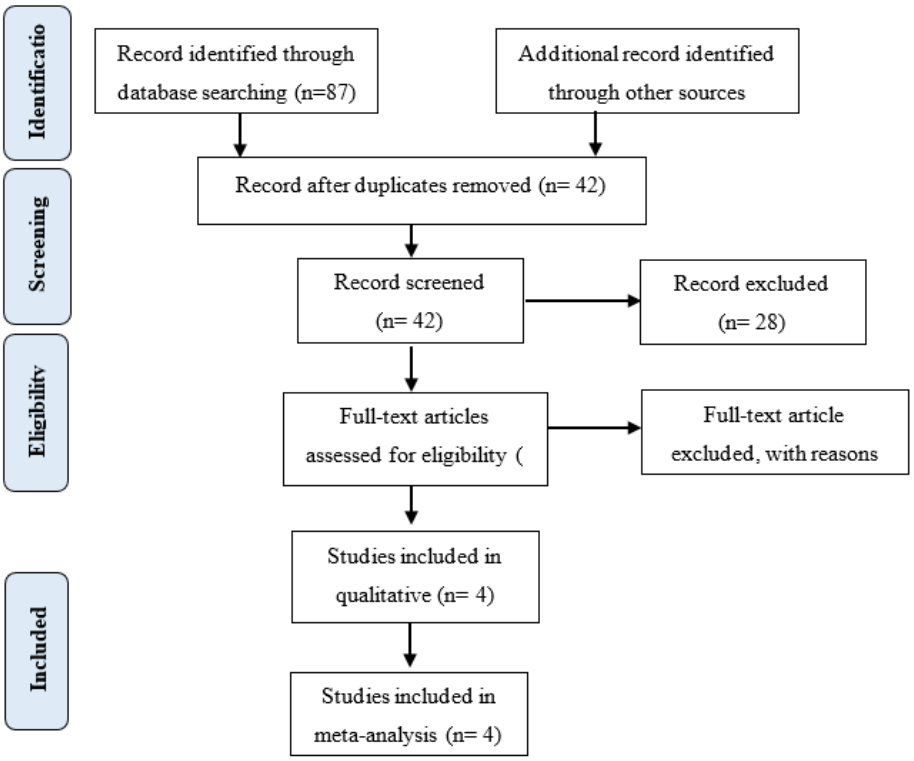


Figure 1. Flow chart of study selection

Inclusion Criteria

Injections of corticosteroids or platelet-rich plasma (PRP) for moderate to severe carpal tunnel syndrome are eligible for inclusion. Many outcomes have been studied, including Visual Analog Scale (VAS), Sensory Peak Latency (SPL), Distal Motor Latency (DML), and Boston Carpal Tunnel Questionnaire Symptom Severity Scale (BCTQ-SSS).

Table 1.
PICO Table Describing Inclusion and Exclusion Criteria

Study Component	Inclusion	Exclusion
Population	• Patients were adults and diagnosed with mild to moderate CTS	• Less than 3 months of follow up • Trauma, degenerative, and oncological pathology • Animal studies
Intervention and Comparison	• Patients were treated with local PRP injection and local Corticosteroid injection	• All other treatments • Surgical treatments
Outcome	• VAS • BCTQ-FSS • BCTQ-SSS • DML • SPL	• No outcome mentioned or different outcomes
Publication	• Primary research published in English in a peer-reviewed journal	• Abstracts, editorials, letters • Duplicate publications of the same study that do not report on different outcomes • Conference presentations or proceedings • Studies in which the relevant data cannot be extracted and the original author is contacted without a response.
Design	• Randomized controlled trials	• Cohort studies • Case reports or series • Review articles

Quality Evaluation

The GRADE Working Group, the Oxford Center for Evidence-based Medicine, and the AHRQ all contributed to the criteria used to evaluate the research's quality and risk of bias. Evaluation of perspicacity was carried out by the GRADE Working Group. Different types of evidence are classified according to their quality: "class I" refers to randomized controlled trials of good quality, "class II" to cohorts of excellent quality or moderate to bad quality, "class III" to case-control studies or cohorts of moderate to poor quality, and "class IV" to case series.

RESULT

Literature Search, Study Selection and Study Characteristics

The computerized study combined through several databases and turned up 87 entries. Once the identification, screening, eligibility, duplicate removal, and exclusion procedures were completed, the remaining four studies were included into the quantitative and qualitative synthesis. Not having data for means and standard deviations led to the elimination of the other papers, which did not fulfill the inclusion and exclusion criteria either.

Table 2.
Studies included in the analysis

No.	Reference	Journal	Study Design	Level of Evidence
1.	Atwa et al., 2019	Elsevier	A Prospective Randomized Controlled Study	I
2.	Senna et al., 2019	Clinical Rheumatology	A Prospective Randomized Controlled Study	I
3.	Hashim et al., 2020	The Egyptian Journal of Neurology, Psychiatry and Neurosurgery	A Prospective Randomized Controlled Study	I
4.	Benny et al., 2022	The Journal of The International Society of Physical and Rehabilitation Medicine	A Prospective Randomized Controlled Study	I

Table 3.
Risk of bias graph of all studies included.

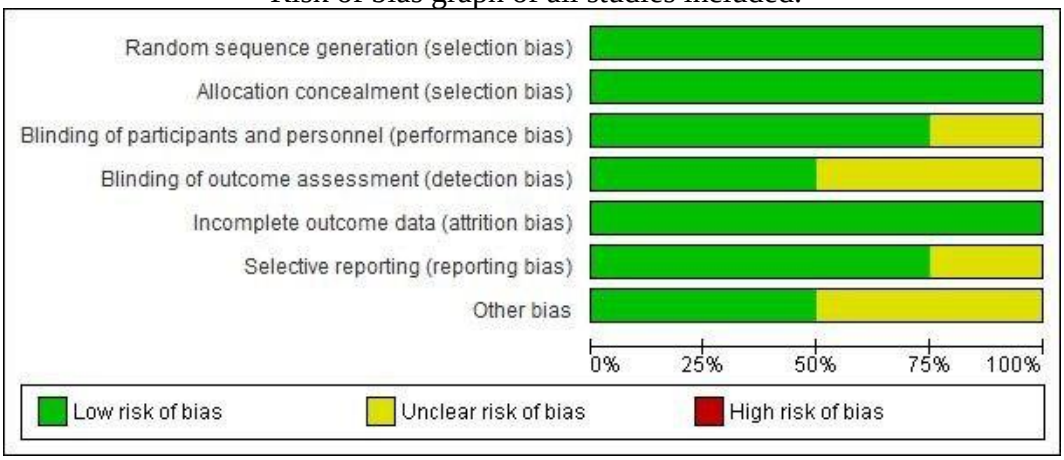
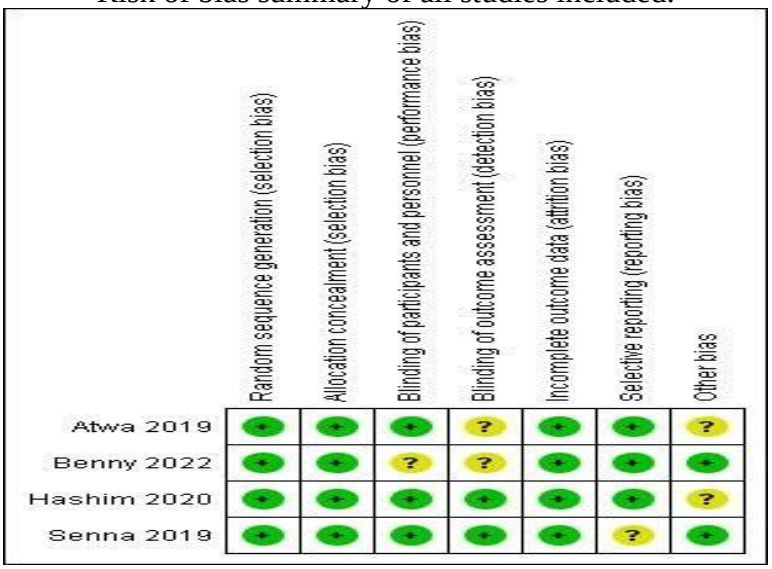


Table 4.
Risk of bias summary of all studies included.



Statistical Analysis

We used Review Manager 5.4 (RevMan; The Cochrane collaboration Oxford, England) software for all statistical analyses. To further analyze the overall findings, we conducted a sensitivity analysis, taking into account the heterogeneity of the present research. Using the I2 statistic, we looked at the degree of heterogeneity among trials and classified it as low (25–50%), moderate (50–75%), or high (>75%). To determine the overall MDs/ORs, we used the fixed-effect models in cases where studies showed little heterogeneity. The random effects concept was used in other instances. Statistical significance was assumed for studies with P values below 0.05. Our meta-analysis results were shown in forest plots.

Outcome Analysis

A total of 245 individuals were included in this meta-analysis; 123 of their patients had platelet-rich plasma injections and 122 received corticosteroid injections. The follow-up period was similar for each study that after one and three month after injection. The main characteristic of include studies (Table 5) and PRP injection (Table 6).

Table 5.
The main characteristics of include studies.

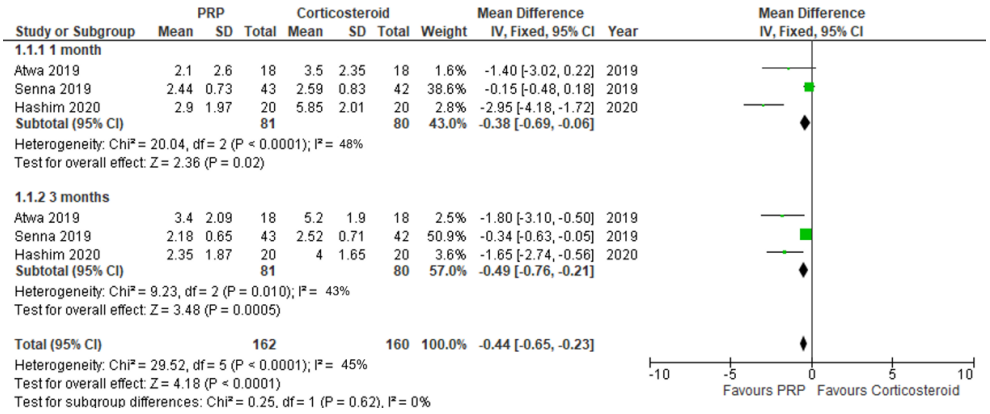
Study (Year)	No. of patients		Male/ Female	Age (Year)		Duration (Month)		Teratment in control group	Outcome measures	Follow-up
	PRP	Control		PRP	Control	PRP	Control			
Benny et al., 2022	42	42	15/69	44.7 ± 8.8	47.0 ± 10.3	NR	NR	1 ml Methyl prednisolone acetate	FSS, SSS	3 months
Hashim et al., 2020	20	20	5/35	48.8 ± 7.45	49.15 ± 6.06	24.1 ± 7.05	23.3 ± 7.26	1 ml Methyl prednisolone acetate	VAS, FSS,SSS DML, SPL	3 months
Atwa et al., 2019	18	18	4/32	38.5 ± 8	36.6 ± 8.8	14 ± 9	19 ± 11	1 ml Methyl prednisolone acetate	VAS, DML, SSS, FSS	3 months
Senna et al., 2019	43	42	14/71	38.3 ± 6.4	40.7 ± 9.4	NR	NR	1 ml Methyl prednisolone acetate	VAS, FSS, SSS DML, SPL,	3 months

Table 6.
The main characteristics Platelet-rich plasma injection.

Study	Activation	Volume (ml)	Centrifuge time	Injection approach	Injection level	Needle size (gauge)
Atwa et al., 2019	Calcium chloride	2	3000 rpm (3 min) then 4000 rpm (15 min)	Ulnar lateral	Proximal carpal	25
Senna et al., 2019	Calcium chloride	2	3000 rpm (3min) then 4000 rpm (15 min)	Ulnar lateral	Proximal carpal	25
Hashim et al., 2020	Sodium citrate	1	1600 rpm (8 min)	Ulnar lateral	Distal carpal	25
Benny et al., 2022	Sodium citrate	1	1000 rpm (4 min)	Ulnar lateral	Proximal carpal	28

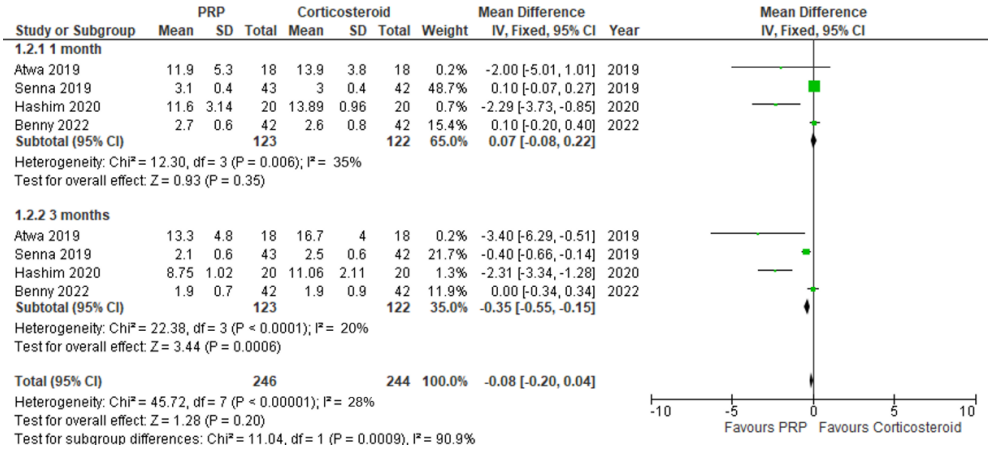
VAS

We divided the patients with carpal tunnel syndrome into two groups: those who had PRP injections and those who had corticosteroid injections. We next compared the VAS outcomes at one and three months. With a mean difference of -0.38 (95% CI -0.69 to -0.06) and a p-value less than 0.05, we found a statistically significant difference between the two groups at the one-month test, favoring PRP injection and making VAS lower . Another finding that is consistent with this is that PRP injection was associated with a lower VAS at 3 months (Mean difference -0.49; 95% CI -0.76 to -0.21; $p < 0.05$). Within subgroup analysis (1 month vs. 3 month), no significant difference was found ($p > 0.05$).(Atwa et al., 2019; Hashim et al., 2020; Senna et al., 2019)



BCTQ-FSS

We divided the patients with carpal tunnel syndrome into two groups: those who had PRP injections and those who had corticosteroid injections. We next compared the VAS outcomes at one and three months. With a mean difference of -0.38 (95% CI -0.69 to -0.06) and a p-value less than 0.05, we found a statistically significant difference between the two groups at the one-month test, favoring PRP injection and making VAS lower . Another finding that is consistent with this is that PRP injection was associated with a lower VAS at 3 months (Mean difference -0.49; 95% CI -0.76 to -0.21; $p < 0.05$). Different result was found in 3 month outcome with significant results for better BCTQ-FSS in favours of PRP injection (Mean difference -0.35; 95% CI -0.55 to -0.15; $p < 0.05$). Within subgroup analysis (1 month vs. 3 month), significant difference was found ($p < 0.05$).(Atwa et al., 2019; Hashim et al., 2020; Reni Benny, Srikumar Venkataraman, Asem Rangita Chanu, U Singh, Devasenathipathy Kandasamy, 2022; Senna et al., 2019)



BCTQ-SSS

In a subgroup study using one-month and three-month time intervals, we determined the BCTQ-SSS outcome for patients with carpal tunnel syndrome when comparing the effects of platelet-rich plasma (PRP) injections vs corticosteroid injections. Our results showed that at the one-month outcome, there was no statistically significant difference between the two groups (Mean difference -0.05; 95% CI -0.24 to 0.14; $p > 0.05$). Different result was found in 3 month outcome with significant results for better BCTQ-SSS in favours of PRP injection (Mean difference -0.22; 95% CI -0.42 to -0.02; $p < 0.05$). Within subgroup analysis (1 month vs. 3 months), no significant difference was found ($p > 0.05$).(Atwa et al., 2019; Hashim et al., 2020; Reni Benny, Srikumar Venkataraman, Asem Rangita Chanu, U Singh, Devasenathipathy Kandasamy, 2022; Senna et al., 2019)

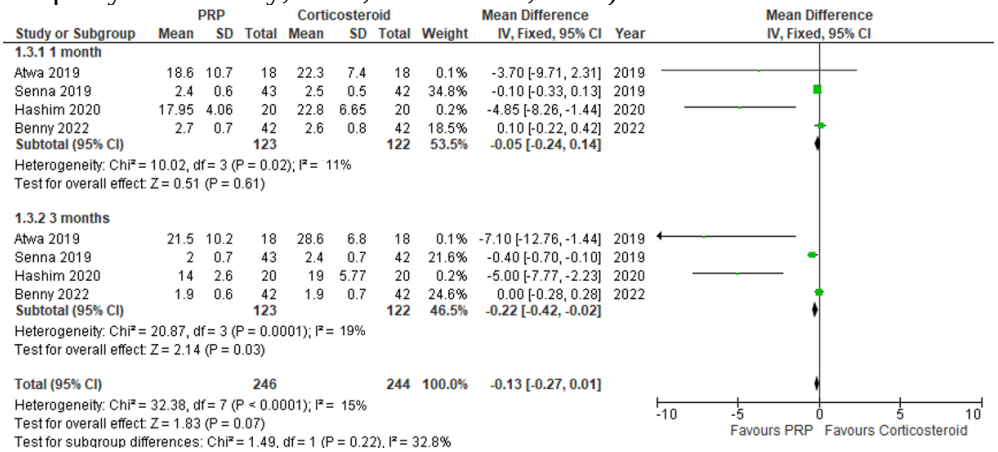
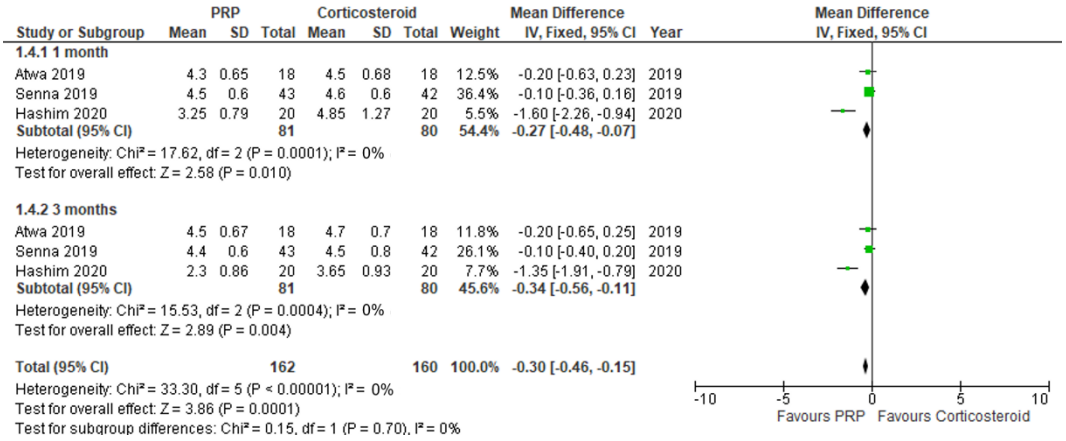


Figure 4. Pooled analysis of BCTQ-SSS outcome

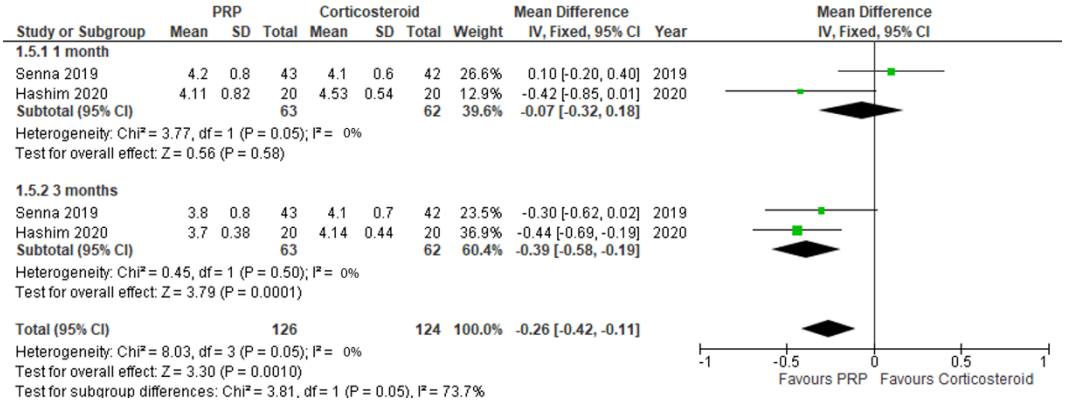
DML

Using a subgroup analysis that encompassed time intervals of one month and three months, we examined the DML results of PRP injections vs corticosteroid injections in patients with carpal tunnel syndrome. With a mean difference of -0.27; 95% CI -0.48 to -0.07; $p < 0.05$), PRP injection demonstrated improved DML at the one-month outcome, indicating a statistically significant difference between the two groups. A similar finding was also seen in the 3-month outcome, favoring PRP injection with improved DML (Mean difference -0.34; 95% CI -0.56 to -0.11; $p < 0.05$). Within subgroup analysis (1 month vs. 3 months), no significant difference was found ($p > 0.05$).(Atwa et al., 2019; Hashim et al., 2020; Senna et al., 2019)



SPL

Subgroup analysis was used to evaluate the efficacy of corticosteroid injections with that of SPL injections given one month and three months subsequent to PRP injections in individuals suffering from carpal tunnel syndrome. Mean difference -0.07; 95% CI -0.32 to 0.18; p > 0.05) at the 1-month outcome did not show a statistically significant difference between the two groups. Different result was found in 3 month outcome with significant results for better SPL in favours of PRP injection (Mean difference -0.39; 95% CI -0.58 to -0.19; p < 0.05). Within subgroup analysis (1 month vs. 3 month), no significant difference was found (p = 0.05).(Hashim et al., 2020; Senna et al., 2019)



DISCUSSION

We used a systematic review and meta-analysis to determine the efficacy of PRP injection in conjunction with corticosteroid injection for patients with mild to moderate CTS. Based on the data obtained after one and three months of follow-up, it was shown that local PRP injection was superior to corticosteroid injection in lowering VAS and DML (Atwa et al., 2019; Hashim et al., 2020; Senna et al., 2019). Local PRP injections also outperformed corticosteroid injections in terms of BCTQ-FSS, BCTQ-SSS (Atwa et al., 2019; Hashim et al., 2020; Reni Benny, Srikumar Venkataraman, Asem Rangita Chanu, U Singh, Devasenathipathy Kandasamy, 2022; Senna et al., 2019) and SPL during the three-month follow-up (Hashim et al., 2020; Senna et al., 2019). In the absence of treatment, the symptoms of CTS would gradually intensify. Aseptic inflammation and permanent nerve damage may occur from long-term ischemia and compression of the median nerve in the carpal tunnel. By effectively reducing the generation of acute inflammatory indicators like CRP and IL-6, a local steroid injection may alleviate pain and inflammation.(Hashim et al., 2020; Peerbooms et al., 2019) Nevertheless, steroid usage increases the risk of neurotoxicity and local soft tissue rupture unrelated to healing and signaling pathway activation.(Kim & Park, 2014; Nepple & Matava, 2009) A large body of research indicates that platelet-rich plasma (PRP) regulates angiogenesis, reduces inflammation, and aids in peripheral nerve regeneration.(Sánchez et al., 2012) Evidence from studies conducted by Zheng et al. demonstrates that PRP, at concentration varying between 2.5% and 20%, considerably accelerates a number of processes.

These include, but are not limited to, the migration and proliferation of Schwann cells in vitro, the release of growth factors such as glial cell line-derived neurotrophic factor and nerve growth factor, and the release of additional growth factors.(Canbin Zheng,Qingtang Zhu,Xiaolin Liu,Xijun Huang,Caifeng He,Li Jiang,Daping Quan,Xiang Zhou, 2013) As shown by Farrag et al., PRP injections into the area around damaged nerve tissue show promise as a bioremediation approach. They showed that using a rat model of facial nerve axotomy, they could speed up nerve transmission, increase the number of axons, and thicken

the myelin sheath by adding PRP during nerve suture.(Tarik Y. Farrag MD, Mohamed Lehar MD, Pauline Verhaegen MS, Kathryn A. Carson ScM, Patrick J. Byrne MD, 2009) The current primary method by which PRP achieves its biological effect is by the activation of platelets, which results in the production of many cytokines. These include vascular endothelial growth factor, platelet-derived growth factor, transforming growth factor, insulin-like growth factor, and many more. Both cell proliferation and tissue healing are profoundly impacted by these cytokines.(Frédéric Picard MD, Barbara Hersant MD, Romain Bosc MD, Jean-Paul Meningaud MD, 2015) By promoting the formation of type α-2 and III collagen in the cells of the flexor support belt, these cytokines may repair damaged MN and reduce pressure in the carpal tunnel all at once.(Allampallam, Krishnan PhD; Chakraborty, Joana PhD; Robinson, 2000)

Compared to the control group, the PRP group had significantly lower VAS and DML ratings at one and three month follow-up, according to our meta-analysis. Three months following the treatment, the PRP group showed substantial improvements in BCTQ-FSS, BCTQ-SSS, and SPL (Atwa et al., 2019; Hashim et al., 2020; Reni Benny, Srikumar Venkataraman, Asem Rangita Chanu, U Singh, Devasenathipathy Kandasamy, 2022; Senna et al., 2019). Our research indicates that PRP takes some time to reach its maximum therapeutic efficacy and that its effects are gradual. While treating plantar fasciitis and external humeral epicondylitis with PRP, a similar occurrence occurred.(G. Merolla, F. Dellabiancia, A. Ingardia, 2015) By reducing ischemia damage to the MN and the associated connective tissue and flexor retinaculum, the hydrodissection action after injection helps alleviate CTS symptoms by removing adhesions and compressing them.(Cass, 2016) Based on these findings, platelet-rich plasma (PRP) works as well as, or even better than, injecting corticosteroids in the short and medium terms. Compared to the control group, the PRP group had substantially lower BCTQ-FSS and BCTQ-SSS scores after three months of follow-up. Among the many benefits of using local PRP injections to treat CTS, the most noticeable of these is the significant improvement in wrist joint function and symptom relief seen in the middle to long term. Therefore, compared to injecting corticosteroids, local PRP injection may be a better and more viable therapy option.

Variations in injection volume and manner of preparation were among the factors taken into account in our meta-analysis. There is no general agreement on how to prepare patients for PRP injections, how much PRP to inject, or what concentration of PRP is best for treating CTS. Our understanding is that there is little to no delay between PRP extraction, preparation, and injection, and that there is little to no effect on outcome markers. While some studies did mention how long it took to prepare the PRP before injecting it, others did not. Different activations used to produce PRP may influence the release of growth factors. (Sophia Harrison, Patrick Vavken, Sherwin Kevy, May Jacobson, David Zurakowski, 2014) Three investigations used a 25 G needle and one used a 28 G needle. Since research has shown that varying needle sizes and calibers have no effect on platelet functioning, smaller needles may be utilized to avoid painful injections of local PRP.(Olivier Bausset, Jeremy Magalon, Laurent Giraudo, Marie-Laure Louis, Nicolas Serratrice, Corrine Frere, Guy Magalon, Françoise Dignat-George, 2004) Furthermore, the included studies show a volume of PRP injections ranging from 1 to 2 ml. As a result, different injection amounts have distinct biological consequences. It is possible that the hydrodissection effect and repairability become more apparent with a greater injection volume. The paucity of published data necessitates further investigations into the ideal amount and level of pretreatment for local PRP injections.

When looking for side effects from local PRP injections, only one study found any. Senna et al. found that paracetamol and local cold were effective in reducing the increased pain perception in the first 48 hours after injection.(Senna et al., 2019) Each study used the ulnar lateral approach. The most successful injection approach for treating carpal tunnel syndrome, according to a Bayesian network meta-analysis, is ultrasound-guided ulnar injection.(Chen et al., 2015) Because of its bioprosthetic properties, platelet-rich plasma (PRP) made from autologous blood lowers the risk of tendon rupture due to local steroid injection, and it also decreases immunological responses. Thus, CTS sufferers can cure their condition with local PRP injection, which is a pretty safe option. Several caveats should be noted about our study. In the first place, the follow-up period is rather brief, and our study only provides a summary evaluation of the short- to mid-term efficacy of local PRP injection. Furthermore, the electrodiagnostic assessments of MN in CTS patients from both the short and medium terms of effectiveness were the only ones reported in this investigation. Thirdly, the sample sizes are somewhat modest, despite the fact that all of the included studies are RCTs. The latest meta-analysis demonstrated that local PRP injection is a superior therapy for CTS, despite the limitations.

CONCLUSION

Our research shows that platelet-rich plasma (PRP) may work better than corticosteroid injection for moderate to mild CTS, and it may also improve median nerve function and discomfort throughout the short to medium term. After PRP injection, electrophysiological indices were somewhat better than after corticosteroid administration. Patients with mild to severe CTS found PRP injection to be an additional therapy that was both effective and safe.

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