Platelet-rich-plasma Injections vs. Corticosteroid Injections in the Reduction of Pain for Patients with Frozen Shoulder: A Critically Appraised Topic

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Clinical Scenario

- Frozen shoulder also known as Adhesive Capsulitis[1]
- 5% of population suffers from frozen shoulder[1,2]
- 4x more likely in women[1,2]
- Recovery is 2-3 years long[1]
- Leading treatment is Corticosteroid injections but fail to provide long term relief[2,4,5]
- PRP injections are new in research[6]
  - Inject extra growth factors and mediators from the alpha granules of the platelets directly into the injury or pathology

Focused Clinical Question

Is platelet-rich plasma or a corticosteroid injection better for relieving pain for patients with frozen shoulder pathologies?

Summary of Search Strategy

Terms:

- P: Frozen shoulder
- I: Platelet-rich plasma injection
- C: Corticosteroid injection
- O: Pain relief

Inclusion Criteria:

- Studies comparing PRP and CS in frozen shoulder
- Studies in the English language
- Studies within the past 5 years (2018-2023)
- Studies with human subjects
- Randomized controlled trials
- Studies using a visual analog scale (VAS)

Exclusion Criteria:

- Case studies
- Cohort studies
- Systematic reviews
- Studies that only used PRP or CS
- Studies that did not present statistical results
- Studies that did not use a visual analog scale for pain as their outcome measure

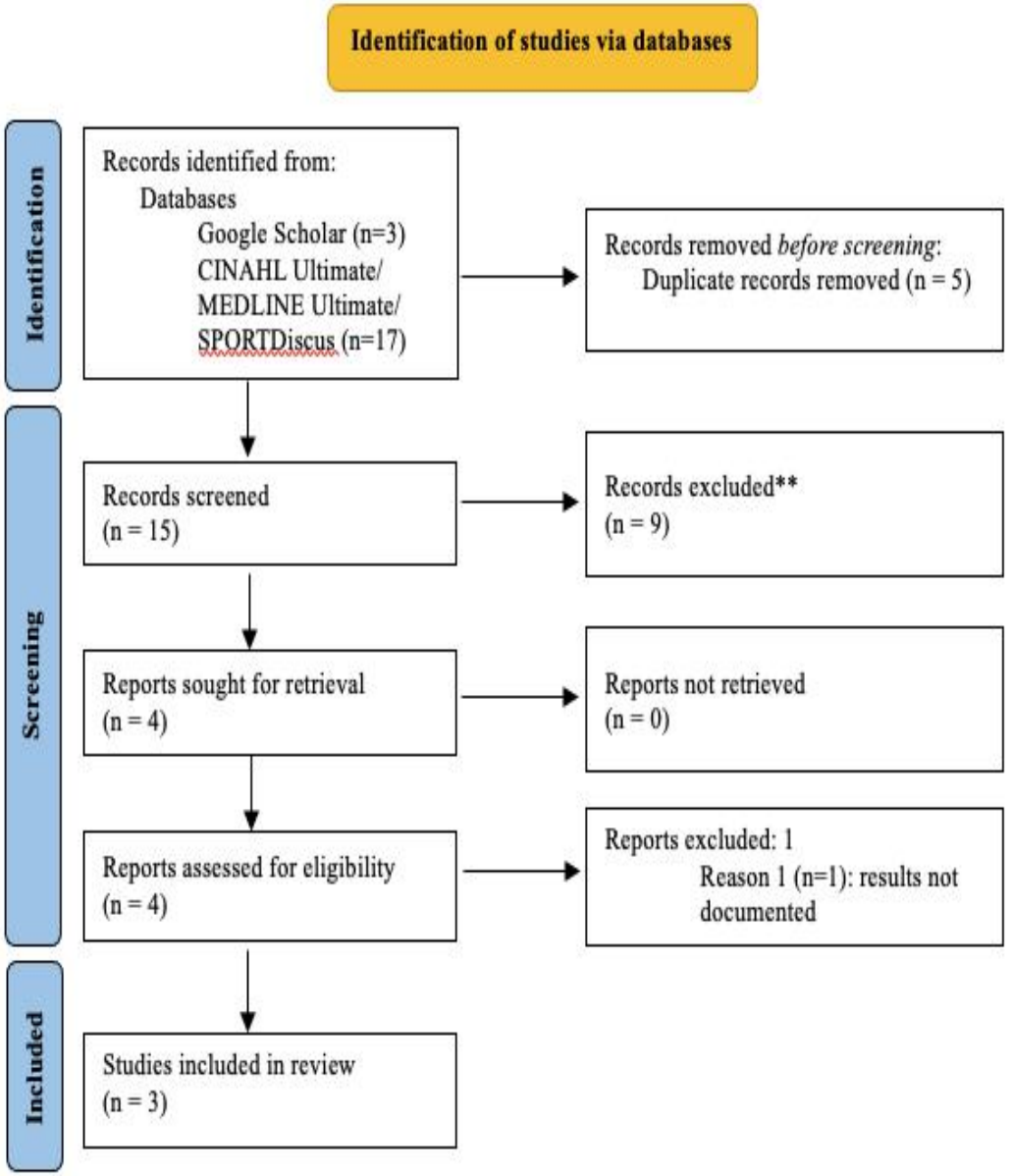

Figure 1 - Search Strategy

PEDro Scale Results[8]

Table 1: Results of PEDro Scale for Each Article

	Somisetty et al.[11]	Gupta et al.[9]	Shahzad et al.[10]
1.Eligibility criteria specified (yes/no)	yes	yes	yes
2. Subjects randomly allocated to groups (yes/no)	yes	yes	yes
3. Allocation was concealed (yes/no)	yes	yes	yes
4. Groups similar at baseline (yes/no)	yes	yes	yes
5. Subjects were blinded to group (yes/no)	no	no	no
6. Therapists who administered therapy were blinded (yes/no)	no	no	no
7. Assessors were blinded (yes/no)	no	yes	no
8. Minimum 85% follow-up (yes/no)	yes	yes	yes
9. Intent to treat analysis for at least 1 key variable (yes/no)	yes	yes	yes
10. Results of statistical analysis between groups reported (yes/no)	yes	yes	yes
11. Point measurements and variability reported (yes/no)	yes	yes	yes
Overall Score (out of 10)	7/10	8/10	7/10

Note: Item 1 was not included in overall score
Abbreviations: PEDro: Physiotherapy Evidence Database score

Summary of Article Evidence

Table 2: Characteristics of Included Studies

	Somisetty et al.[11]	Gupta et al.[9]	Shahzad et al.[10]
Study Design	Randomized, controlled trial	Randomized, double-blinded controlled trial	Randomized, controlled trial
Participants	N = 68 patients from 18-75 with a mean age of 58.3 ± 8.1 years (IA PRP group) and 58.5 ± 7.7 years (IA CS group); 15 (44.12%) males and 19 (55.88%) females (IA PRP group) and 20 (58.82%) males and 14 (41.18%) females (IA CS group)	N = 60 patients with periarthritis shoulder; with a mean age of 46.7 ± 7.13 years (Triamcinolone group) and 47.8 ± 9.56 years (PRP group); 13 males and 17 females (Triamcinolone group) and 12 males and 18 females (PRP group)	N = 202 with a mean age of 70.41 ± 4.67 years (group A) and 57.0 ± 7.74 years (group B); 41.38% males and 56.82% females (group A) and 40.91%) males and 59.09% females (group B)
Interventions Investigated	1. 4 mL PRP injection 2. 2 mL (80mg) methylprednisolone acetate mixed with 2 mL normal saline injection	1. 2 mL of triamcinolone (40mg/mL) injection 2. 2 mL autologous PRP injection which was centrifuged in two spins with 0.9% sodium citrate. The first spin was at 1,500rpm for 15 minutes and the second spin was 2,500 rpm for 10 minutes. Supernatant was discarded, 3 mL of substance was taken into syringe with 0.1 mL of calcium chloride.	1. 2 mL PRP injection 2. 2 mL (80mg) methylprednisolone acetate
Outcome Measures	Patients were assessed at the end of 2, 4, 8, 12, and 24-weeks post injection. Specific measures include VAS, QuickDASH, SPADI measures. These were completed to assess pain perception as well as overall shoulder functionality.	Patients were assessed at the end of 4th, 12th, and 24th weeks post injection. Specific measures include VAS and QuickDASH measures. These were completed to assess pain perception as well as overall shoulder functionality.	Patients were assessed pre- and post-injection (12 weeks). Specific measures include VAS and UCLA measures. ROM was also assessed using a goniometer in the anteroposterior and lateral planes of motion. These were completed to assess pain perception as well as overall shoulder functionality.

Summary of Article Evidence (cont.)

Main Findings (Raw data seen in Table 3)	All data was organized through Microsoft Excel and then analyzed via SPSS version 24.0. Independent t-tests were used on SPSS to find the normality of distribution of groups. If a group was non-normally distributed, a Mann-Whitney U test was used. Overall, $p = <0.05$ was used as the significance value for all statistics. The scores at pre-injection and 8 weeks were not statistically significant, while the post-injection, 2,3, 12, and 24 weeks were all found to have a significant statistical difference.	Data was analyzed through SPSS version 24 and unpaired t-tests were used for analyzing the continuous variables used. Both the Fisher's exact test and Pearson's chi-square test were used to analyze categorical variables. The significance value used was $p = <0.05$. Within the first 4-12 weeks the data showed a significant improvement of VAS score for those with a CS injection over those with the PRP injection. However, after 24 weeks the PRP injection groups showed a significant difference in VAS scores over those with the CS injection.	All scores were analyzed via independent t-test for significance through SPSS version 20 and used $p = 0.05$ as their significance value. Overall their findings showed a significant improvement in ROM and functionality of group A (PRP) over group B (CS).
Level of Evidence	1b	1b	1b
Validity Score	PEDro 7/10	PEDro 8/10	PEDro 7/10
Conclusion	Patients within group 1 (PRP) showed better outcomes in pain reduction, improved ROM, and improved quality of life and ability to perform activities of daily living. PRP had better long-term outcomes over CS.	After week 4, patients in group 1 (CS), expressed less pain, saw greater amounts of ROM, and functionality than those in group 2 (PRP). Post week 12 scores for group 1 (CS) showed less pain than group 2 (PRP), but also showed less functionality than group 2 (PRP). Finally, after week 24, group 1 (CS) displayed more pain and less functionality than seen in group 2 (PRP).	Patients within group 1 (PRP) showed substantial improvement in pain scores, UCLA, and ROM measurements than that of group 2 (CS) during post-injection measurements

Abbreviations: PRP: platelet rich plasma; IA: intra-articular; CS: corticosteroid; VAS: visual analog scale; QuickDASH: condensed version of disabling conditions of the arm, shoulder, and hand score[11]; SPADI: shoulder pain and disability index; ROM: range of motion

Summary of Article Evidence (cont.)

Table 3: Mean VAS Scores and P-values

	Pre - injection	Immediate post-injection	Week 2	Week 4	Week 8	Week 12	Week 24
PRP							
Gupta et al.	67.4	-	-	51.7	-	43.23	14.33
Shahzad et al.	8.9	-	-	-	-	0.85	-
Somisetty et al.	8.5	7.0	6	5	4	2	1
CS							
Gupta et al.	69.63	-	-	46.27	-	31.83	31.63
Shahzad et al.	9.5	-	-	-	-	2.3	-
Somisetty et al.	8	6.0	5	5	4	3	2
P-value							
Gupta et al.	0.136	-	-	0.0048*	-	0.0001*	0.0001*
Shahzad et al.	0.06	-	-	-	-	0.004*	-
Somisetty et al.	0.1439	-	-	0.0021*	0.4766	0.0011*	0.0011*

* Denotes statistical significance

Clinical Bottom Line

- **Grade A evidence:**
  - PRP injections significantly decreased VAS scores compared to CS injections for long term results

- **Short term results were inconclusive**

Discussion

- **Similarities between studies:**
  - All RCT
  - All studies used matching amount of fluid in their injections
    - Gupta et al. and Shahzad et al. used 2ml of PRP and 2ml of CS
    - Somisetty et al. used 4 ml of PRP and 2ml of CS mixed with 2ml of saline

- **Differences between studies:**
  - Different corticosteroids used (2 methylprednisolone acetate, 1 triamcinolone)
  - Outcome measures – health related quality of life questionnaires
    - DASH, quick DASH, SPADI, UCLA

Comparison to Other Pathologies

- Hamstring strains[12]
- Osteoarthritis (knee)[13]
- Rotator Cuff disease[14]

All studies on other pathologies showed a greater decrease in VAS scores overall for PRP than CS, however, their findings were not statistically significant.[12-14]

Implications for Clinical Practice and Future Research

- More Research!
- Standardize outcome measures
- Focused demographics
  - age and activity level
- Importance of patient-centered care

- For short-term pain relief, clinicians should consider CS injections over PRP injections
- For long term pain relief, clinicians should follow evidence-based practice and utilize PRP injections over CS injections

Acknowledgements

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Abstract

Clinical Scenario: Frozen shoulder affects 5% of the population, causing pain and stiffness lasting up to 3 years.[1] Fibrosis causes loss of function of the shoulder joint 4 times more in females than males and in about 20% of individuals with diabetes mellitus.[1,2] Corticosteroid injections are currently the most common treatment injection but have not yet been compared to platelet-rich plasma injections. ***Focused Clinical Question:*** Is platelet-rich plasma (PRP) or a corticosteroid (CS) injection better for relieving pain for patients with frozen shoulder pathologies? ***Summary of Key Findings:*** Two articles found that VAS scores significantly decreased more in PRP injections than in CS injections in both short- and long-term tests. One study found that CS injections during the short-term tests had a greater decrease in VAS scores than PRP, and then during the long-term, PRP decreased more than CS injections. ***Clinical Bottom Line/Strength of Recommendation:*** Grade A evidence found that PRP injections had significantly decreased visual analog scale (VAS) scores compared to CS for long-term results.[3] Evidence was inconclusive for short-term benefits.

Keywords: platelet-rich-plasma injection, corticosteroid injection, frozen shoulder, visual analog scale, adhesive capsulitis

Clinical Scenario

Frozen shoulder also known as adhesive capsulitis, is a painful condition affecting the shoulder, limiting range of motion due to stiffening.[1] Around 5% of the population is affected by frozen shoulder with females 4 times as likely to suffer from the condition than males and individuals with Diabetes mellitus having a prevalence of frozen shoulder at 20%.[1,2] In patients with frozen shoulder, fibrosis of the glenohumeral joint builds up for over 3 months and goes away slowly, causing a 2-3 year recovery time for patients.[1] Due to this long recovery time, treatment methods that may provide faster relief are imperative to examine.

Currently, there is no agreement on the best treatment for frozen shoulder with 4 conservative treatments (NSAIDs, physical therapy, hydrodistension, and corticosteroid injections) and 2 surgical methods (Manipulation under anesthesia and arthroscopic capsular release) being popularly used.[2,4] Operative treatment is typically used after patients have not found relief from conservative methods in 3-6 months.[4] Corticosteroid injections are the leading treatment to provide pain relief for patients but fail to maintain results long term.[2,4,5] Within the last decade, research on the use of Platelet-rich plasma injections and frozen shoulder has been conducted, providing a new treatment option for the pathology.[6] Platelet-rich plasma is autologous human blood that has been centrifuged to concentrate the platelet count.[7] On average, a human has a platelet count from 150,000 to 300,000/microliter.[7] For a PRP injection, the platelet count is increased to up to 1,000,000/microliter.[7] Included in the PRP injection are the growth factors and mediators in the alpha granules of the platelets.[7] By doing this, a higher than natural amount of these factors of healing can be placed directly into an injury or pathology.[7]

Corticosteroid injections do not provide long-term relief for patients with frozen shoulders, a pathology that often has a multi-year recovery time.[2] Research on new treatment methods such as a PRP injection that could provide this long-term relief is necessary.[2] Currently, there is no compilation or analysis of evidence on the research between the two treatment methods discussed. The purpose of this study is to compare corticosteroid injections and platelet-rich plasma injections in their treatment of pain caused by a frozen shoulder.

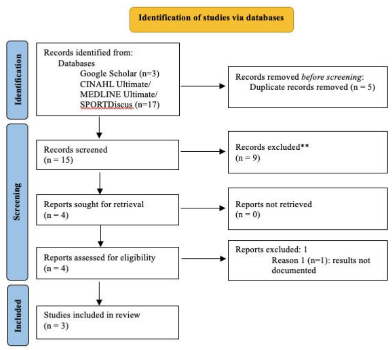
Summary of Search Strategy

To identify relevant research papers, Boolean searches were conducted on Google Scholar, CINAHL Ultimate, MEDLINE Ultimate, and SPORTDiscus databases. Key terms used were corticosteroid (CS) injection, platelet-rich plasma (PRP) injection, frozen shoulder, and adhesive capsulitis. Database searches were conducted from September 14th through September 25th, 2023. (Figure 1) The terms used to guide the search strategy, following the PICO format, were: P: frozen shoulder, I: Platelet-rich plasma injections, C: corticosteroid injections, and O: pain relief measured on a VAS scale. Studies were limited to randomized control trials written in English within the past 5 years that used human subjects to compare PRP vs CS injections and the relief of pain from frozen shoulder measured with a VAS. Excluded studies include case studies, cohort studies, systemic reviews, studies that did not test both interventions or use the selected outcome measure, and studies that did not present their statistical results.

Three relevant research studies were selected using these search terms. The validity of the selected studies was determined using the PEDro scale (Tables 1 and 2).

Each article selected summarized outcome measures (VAS scores) in a table, chart, or graph. For statistical analyses, all studies selected used a p-value of < 0.05 to determine statistical significance. The article scores from the PEDro scale are as follows: 8/10[9], 7/10[10], and 7/10[11]. All articles lacked blinding of the participants and the therapist who administered the treatment. Two articles lacked blinding of the assessors as well.

Figure 1 – Search Strategy



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5. Subjects were blinded to group (yes/no)	no	no	no
6. Therapists who administered therapy were blinded (yes/no)	no	no	no
7. Assessors were blinded (yes/no)	no	yes	no
8. Minimum 85% follow-up (yes/no)	yes	yes	yes
9. Intent to treat analysis for at least 1 key variable (yes/no)	yes	yes	yes
10. Results of statistical analysis between groups reported (yes/no)	yes	yes	yes
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Main Findings (Raw data seen in Table 3)	All data was organized through Microsoft Excel and then analyzed via SPSS version 24.0. Independent t-tests were used on SPSS to find the normality of distribution of groups. If a group was non-normally distributed, a Mann-Whitney U test was used. Overall, p = <0.05 was used as the significance value for all statistics. The scores at pre-injection and 8 weeks were not statistically significant, while the post-injection, 2,3, 12, and 24 weeks were all found to have a significant statistical difference.	Data was analyzed through SPSS version 24 and unpaired t-tests were used for analyzing the continuous variables used. Both the Fisher's exact test and Pearson's chi-square test were used to analyze categorical variables. The significance value used was p = <0.05. Within the first 4-12 weeks the data showed a significant improvement of VAS score for those with a CS injection over those with the PRP injection. However, after 24 weeks the PRP injection groups showed a significant difference in VAS scores over those with the CS injection.	All scores were analyzed via independent t-test for significance through SPSS version 20 and used p = 0.05 as their significance value. Overall their findings showed a significant improvement in ROM and functionality of group A (PRP) over group B (CS).
Level of Evidence	1b	1b	1b
Validity Score	PEDro 7/10	PEDro 8/10	PEDro 7/10
Conclusion	Patients within group 1 (PRP) showed better outcomes in pain reduction, improved ROM, and improved quality of life and ability to perform activities of daily living. PRP had better long-term outcomes over CS.	After week 4, patients in group 1 (CS), expressed less pain, saw greater amounts of ROM, and functionality than those in group 2 (PRP). Post week 12 scores for group 1 (CS) showed less pain than group 2 (PRP), but also showed less functionality than group 2 (PRP). Finally, after week 24, group 1 (CS) displayed more pain and less functionality than seen in group 2 (PRP).	Patients within group 1 (PRP) showed substantial improvement in pain scores, UCLA, and ROM measurements than that of group 2 (CS) during post-injection measurements

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Somisetty et al.	0.1439	-	-	0.0021*	0.4766	0.0011*	0.0011*

* Denotes statistical significance

Clinical Bottom Line

Overall, this Grade A evidence found that PRP injections had significantly decreased VAS scores compared to CS for long-term results.[3] However, evidence was inconclusive for short-term benefits. All three articles used within this CAT were randomized control trials, with one of them being double-blinded. The findings of these studies show just how important it is for research on PRP versus CS injections for patient pain reduction as well as overall functionality. It is important to research more both with short- and long-term patient outcomes in mind. Clinicians can use this information to educate themselves and their patients that CS injections are not the only choice for the treatment of their frozen shoulder and other pathologies. Based on this CAT, the suggestion is that corticosteroid injections be used when short-term results are the goal. If long-term results are preferred, then PRP injections are the more effective method.

Discussion

The purpose of this Critically Appraised Topic was to compile the known evidence regarding the effect of Platelet-rich plasma and Corticosteroid injections on frozen shoulder. Using these data, recommendations regarding the treatment of frozen shoulders in a clinical setting can be given. The three randomized control trials selected for this CAT presented results that PRP injections significantly improve frozen shoulder pain more effectively than CS injections in long-term timelines. At 24 weeks, the article by Gupta et al. found VAS scores for a PRP injection to be half of what the scores were for CS injections.[9] Similar results were found in the Somisetty et al. study, which also found that PRP injections had a VAS score half of what the CS injections provided.[11] For the short term (less than 12 weeks), there was disagreement between the studies on whether a steroid injection or PRP injection would be most effective. The study by Gupta et al. found a significant difference favoring CS injections at 4 and 12 weeks but a difference favoring PRP injections at 24 weeks.[9] Shahzad et al. found a significant difference favoring PRP at 12 weeks. Somisetty et al. found a significant difference favoring PRP at week 12 and 24.[10,11]

The three studies used in this CAT were all randomized control trials. In the study conducted by Gupta et al., unlike the other studies, blinding of the assessor was incorporated in addition to just concealment of the allocation.[9] All three articles did not have blinding of the participants or blinding of the therapists.[9–11] Being able to fully blind the study is seemingly unavoidable due to the nature of the study, and the involvement of injections.

Within each study, the amount of fluid injected into the joint capsule was the same.[9–11] Gupta et al. and Shahzad et al. used 2 ml for both the PRP and corticosteroid injections.[9–10] Somisetty et al. used 4 ml of PRP and 2 ml of corticosteroid mixed with 2ml of saline.[11] Unlike the PRP injections, there was more variation in the type of CS used. In the studies by Somisetty et al. and Shahzad et al., the corticosteroid used was methylprednisolone acetate.[10,11] Gupta et. al used triamcinolone for the injections.[9] For the location of the injection, the study by Somisetty et al. stated that an intra-articular injection was used.[11] Shahzad et al. stated that an intra-articular injection was used on the anterior shoulder with no ultrasound guidance.[10] Gupta et al. did not state any details regarding the location of the injection.[9]

For post-injection evaluation the Gupta et al., study used a Disability of Arm, Shoulder, and Hand (DASH) score to evaluate the function of the shoulder and a VAS score for pain.[9] The study by Somisetty et al. used a quickDASH score for function, a VAS scale for pain, and a Shoulder pain and disability index (SPADI) score for pain and function.[11] For both studies mentioned, the DASH score favored the PRP injection.[9,11] Gupta et al., presented a significant difference with a p-value of 0.0001 for the PRP over the CS injection in the DASH score.[9] Shahzad et al., used a University of California at Los Angeles Shoulder Score (UCLA) in addition to the VAS scale to test pain and function.[10] During the post-injection evaluation, a significant difference (p-value=0.002) was found in favor of the PRP injection over the CS injection in the UCLA test.[10]

Implications for Clinical Practice and Future Research

- Other studies on different pathologies such as hamstring strains, osteoarthritis of the knee, and rotator cuff disease showed slight favorability toward PRP over CS injections, but a statistically significant difference was not found; therefore, their results were inconclusive.[12–14]
- For short-term pain relief, clinicians should consider CS injections over PRP injections.
- For long-term relief, clinicians should follow evidence-based practice and utilize PRP injections over CS injections.
- For both treatment timelines, clinicians should reference newly published evidence as more studies are conducted on this topic.
- Limitations of the included studies were the lack of consistent outcome measures, lack of clinical focus on either short or long-term outcomes, and lack of a defined age range.
- Further research should include the following: standardized outcome measures, more focused duration of study, and more specific subject demographics.

References and Acknowledgments

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