Randomized Controlled Trial

Comparison of the Effects of Normal Saline, Hypertonic Saline, and Hyaluronidase on Patients with Postoperative Relapse of Carpal Tunnel Syndrome: A Randomized Controlled Trial

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Ethical Approval: Our study's protocol was approved by the Medical Ethics Committee of Mazandaran University of Medical Sciences at Emam Khomeini Hospital, Sari, Islamic Republic of Iran (registration ID: IR.MAZUMS.REC.1403.310). The research procedure was explained to the patients and, in the case of underage participants, to their parents or legal guardians, and written informed consent was obtained from all.

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Background: Recurrent carpal tunnel syndrome affects up to 25% of patients following surgical decompression, causing significant therapeutic challenges. Hydrodissection, a minimally invasive technique that alleviates perineural adhesions, has shown promise for symptom relief. However, optimal injectable agents for hydrodissection in postoperative relapse of carpal tunnel syndrome remain under investigation.

Objectives: Our study aimed to compare the clinical efficacy of 3 injectable treatments—normal saline, hypertonic saline, and hyaluronidase—in ultrasound-guided hydrodissection for patients with postoperative relapse of carpal tunnel syndrome.

Study Design: A randomized controlled trial with a 12-month follow-up.

Setting: Our study was conducted at Imam Hospital Center in Sari, Islamic Republic of Iran.

Methods: Ninety patients aged 18–60 years, experiencing carpal tunnel syndrome relapse within 6 months postsurgery, were randomly assigned to 3 equal groups (n = 30) to receive ultrasound-guided hydrodissection with either hyaluronidase (300 IU) combined with methylprednisolone, bupivacaine, and normal saline; hypertonic saline (5%) with methylprednisolone and bupivacaine; or normal saline with methylprednisolone and bupivacaine. Patients were followed at postinjection months 3, 6, and 12. Assessed outcomes included the Visual Analog Scale (VAS) for pain, Symptom Severity Scale, patient satisfaction, and the number of required reinjections.

Results: All 3 groups had statistically significant improvements in pain and function ($P < 0.05$). However, the hyaluronidase group had statistically significant greater reductions in VAS and Symptom Severity Scale scores at all follow-up points compared to the other 2 groups ($P < 0.01$). Additionally, this group required fewer reinjections and reported the highest satisfaction rates throughout the study period. There were no statistically significant differences between the hypertonic and normal saline groups in terms of pain, function, satisfaction, or reinjection frequency.

Limitations: Including methylprednisolone in all injection treatments may have confounded the independent effects of the tested agents. The single-center design limits generalizability, and objective imaging or electrophysiological evaluations were not used. The follow-up period was limited to 12 months, leaving long-term outcomes unexplored.

Conclusions: Ultrasound-guided hydrodissection using hyaluronidase statistically significantly improves pain, symptom severity, and patient satisfaction in cases of postoperative relapse of carpal tunnel syndrome and reduces the need for reinjections compared to hypertonic or normal saline. Hyaluronidase appears to be a superior adjunct in hydrodissection procedures and may offer a cost-effective and clinically advantageous approach for managing postoperative relapse of carpal tunnel syndrome.

Key words: Carpal tunnel syndrome, hyaluronidase, hypertonic saline, hydrodissection, postoperative relapse, Visual Analog Scale

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Carpal Tunnel Syndrome (CTS) is a condition characterized by the compression of the median nerve at the wrist, leading to noticeable symptoms. It affects approximately 3.8% of the population, with an annual incidence rate of 276 cases per 10,000 person-years (1). Various risk factors have been identified for this condition (2), including diabetes (3), high blood pressure (4), hormonal changes such as menopause and pregnancy (5), and thyroid dysfunction (6). Additionally, Schreiber and colleagues (4) showed that these risk factors are significantly associated with CTS.

Various studies have been conducted to investigate the efficacy of nonsurgical methods for treating CTS. Atroshi and colleagues (7) showed that corticosteroid injections improve CTS symptoms (7). Furthermore, other studies have shown that injections, coupled with ultrasound guidance, are more effective (8,9). In a controlled randomized trial, researchers reported that local lidocaine injections reduce symptoms and improve electrophysiological status (10). It has also been shown that corticosteroid injections are more effective compared to nonsteroidal anti-inflammatory drugs (11,12).

In addition to nonsurgical treatments, surgical methods are also available to improve CTS. Carpal tunnel release is recommended for patients with persistent symptoms who have not responded to nonsurgical treatments or who opt to skip them. Surgery is a proven and effective solution for carpal tunnel syndrome (13). Surgical treatment procedures involve cutting the transverse carpal ligament and relieving pressure on the contents of the carpal tunnel. Both open CTS surgeries, with or without antebrachial fascia release, have similar clinical and functional outcomes (14). It has been observed that endoscopic surgery results in a slightly shorter postoperative recovery period and faster return to normal wrist function (15). However, endoscopic release can be associated with a higher risk of nerve damage (12). Furthermore, meta-analysis results have shown that endoscopic release is associated with fewer minor complications (such as infection) compared to open surgery, but there is no statistically significant difference between open and endoscopic surgery regarding major complications (such as complex regional pain syndrome) (16). For persistent or recurrent CTS, some nonsurgical treatments are recommended; if symptoms do not improve, repeat carpal tunnel surgery may be necessary (17).

However, patient satisfaction with carpal tunnel release is not universal. Due to the relatively high procedure rate, unsuccessful carpal tunnel release cases are common (18). Long-term studies indicate generally positive outcomes for carpal tunnel release, with clinical success rates ranging from 75% to 90%. This suggests that recurrent postsurgery CTS occurs in approximately 10% to 25% of cases (19).

CTS carries a substantial socioeconomic burden due to its effects on productivity, functional capabilities, quality of life, and the considerable costs associated with its treatment and management (20). Unsuccessful carpal tunnel release can result in significant patient morbidity and dissatisfaction, making it challenging for surgeons to manage. Additionally, failed carpal tunnel release can be a cause of medical malpractice litigation, with settlements exceeding $300,000 (21).

Hyaluronidase, an enzyme known for enhancing the delivery and efficacy of local anesthetics, has emerged as a potential adjunct treatment in CTS surgery. By breaking down hyaluronic acid in the extracellular matrix, hyaluronidase facilitates better infiltration of anesthetics, which may lead to reduced postoperative pain and improved recovery experiences (22,23). Studies have shown that its use can significantly alleviate pain levels and improve functional outcomes, particularly when used in ultrasound-guided injections (22,23).

Despite the promising role of hyaluronidase for managing postoperative pain, its incorporation into clinical practice remains under investigation, as varying results regarding its efficacy have been reported. Some studies indicate that while a majority of patients benefit from its use, a significant number still experience unresolved symptoms, necessitating ongoing research to identify optimal treatment protocols and the patient-specific factors that influence outcomes (25,26). Thus, understanding the effect of hyaluronidase on postsurgical pain and residual symptoms is crucial for improving the quality of care for patients undergoing CTS surgery. This topic continues to generate interest due to its implications for surgical practices and patient satisfaction. As research evolves, integrating hyaluronidase into standard postoperative protocols may transform how pain and residual symptoms are addressed in the context of CTS surgery, potentially leading to more effective pain management and enhanced quality of life for these patients (22,23,26)

Using hyaluronidase with a saline solution for carpal tunnel treatment is considered an effective technique. This approach provides rapid pain relief,

enhances functional improvements, and leads to better median nerve conduction in patients with CTS (26).

Hypertonic saline can be beneficial in some epidural intervention methods for pain management for certain neuropathies (27-29). Additionally, various studies have shown that when hypertonic saline is used as an adjuvant in treatment-resistant chronic radiculopathy, the intervention's effects can last for at least 3 months (30,31). In patients suffering from potential neuropathic pain, the adjunctive administration of hypertonic saline during a lumbar epidural intervention can alleviate pain for a minimum of one month.

Since noninflammatory fibrosis of the subsynovial connective tissue is the most common pathological change in CTS (32,33), which increases the pressure on the median nerve, it is expected that performing the process of prolotherapy (injecting a dextrose solution) would lead to changes in the subsynovial connective tissue and reduce the pressure on the nerve and the associated pain (34).

Bupivacaine is a commonly used local anesthetic, particularly in obstetrics. It works by blocking sodium channels, which slows down the production and transmission of nerve signals. However, it can cause oxidative stress, which may lead to cell death (35,36).

While corticosteroid injections and endoscopic surgery have been shown to alleviate CTS symptoms, the long-term effects and comparative efficacy of alternative treatments such as hyaluronidase injections remain unclear. Our study aimed to address this gap by evaluating the efficacy of hyaluronidase hydrodissection compared to normal saline and hypertonic saline injections.

Methods

Our study was a randomized controlled trial (with the normal saline group serving as the control) that was carried out at Sari_Imam Hospital Center, Islamic Republic of Iran.

Inclusion criteria were: patients aged 18 to 60 with a history of CTS surgery within the previous 6 months and currently experiencing at least 6 of the following symptoms: 1) a decreased range of motion in the hand; 2) Numbness in fingers; 3) burning pain; 4) tparesthesia in fingers, especially the thumb, index, and middle fingers; 5) pain or numbness worsening at night, disrupting sleep; 6) weakness when gripping objects with one or both hands; 7) pain or numbness in hands; 8) feeling of swelling in the fingers.

Exclusion criteria were: 1) CTS due to systemic conditions such as pregnancy, illness, or acromegaly; 2) other diseases, including rheumatoid arthritis, osteoarthritis, gout, or psoriatic arthritis; 3) sensitivity or allergy to the medications to be used in the study; 4) dissatisfaction with an injection at any stage of treatment.

Patients enrolled in the study had CTS for a minimum of 6 months. They had not responded to conservative treatments such as vitamin B complex, nonsteroidal anti-inflammatory drugs, oral steroids, and/or using night splints.

Following the explanation of the research benefits and potential side effects to the patients, informed written consent was obtained from them. Our method of randomization was conducted using IBM SPSS Statistics 20.0 software (IBM Corporation), ensuring patients were evenly assigned to one of the 3 study groups.

We conducted preinjection skin allergy tests for hyaluronidase, methylprednisolone, and bupivacaine.

All injections were performed by a single, experienced provider who utilized the same hydrodissection technique across all patient groups. The procedure was performed using the freehand one-man technique, where the physician simultaneously holds both the syringe and the ultrasonography probe. Continuous ultrasonographic monitoring ensured the needle tip was visible at all times.

Hyaluronidase was administered under sterile conditions. A 26-G needle was inserted from the lateral side toward the midline using an in-plane approach in order to precisely target the median nerve within the carpal tunnel (25). The injection was administered gradually, and the needle was gently advanced, separating the flexor retinaculum from the median nerve through the gradual infiltration of the injectate. Study patients did not receive formal occupational therapy as part of their postinjection care.

The patients were divided into 3 intervention groups: hyaluronidase (n = 30), hypertonic saline (n = 30), and normal saline (n = 30). All procedures were performed under ultrasound guidance.

In the hyaluronidase group, an injectate of one mL of 40 mg methylprednisolone, 1 mL of hyaluronidase (300 IU), 1 mL of bupivacaine, and 1 mL of normal saline was administered around the wrist and along the median nerve.

In the hypertonic saline group, an injectate of 1 mL of 40 mg methylprednisolone, 1 mL of 5% hypertonic saline, 1 mL of normal saline, and 1 mL of bupivacaine was administered around the wrist and along the median nerve.

The normal saline group underwent the same procedure with an injectate of 1 mL of 40 mg methylprednisolone, 2 mL of normal saline, and 1 mL of bupivacaine.

Patients were followed for one year (with follow-ups at 3, 6 and 12 months) for paresthesia For patients experiencing symptom recurrence, additional injections were administered; the number of injections in each group at specific time intervals was recorded.

Pain and disability were assessed using the Visual Analog Scale (VAS) and Symptom Severity Scale (SSS) scores at 4 different time points: preinjection and postinjection months 3, 6, and 12. VAS) is a 10-centimeter straight line with two endpoints: "no pain" (0 cm) on the left and "worst possible pain" (10 cm) on the right. The patient marks a point on the line that represents their pain level. The distance from the left endpoint to the mark is measured in millimeters or centimeters.

Patient satisfaction was assessed at postinjection months 3, 6, and 12. If a patient was satisfied with the ability to perform activities of daily living, it was recorded as acceptable. If the patient was dissatisfied and found the ability to perform activities of daily living unacceptable, this was also noted.

The number of patients who reported pain levels based on a VAS score < 4 was recorded at postinjection months 3, 6, and 12. Additionally, the frequency of patients seeking re-injection for pain reduction was measured at postinjection months 3, 6, and 12.

Statistical Analysis

Data analyses were performed using IBM SPSS Statistics 20.0. The normality of quantitative data was assessed using the Kolmogorov–Smirnov test. Demographic and clinical characteristics are presented as mean (SD) for continuous variables. Quantitative data were compared within and between groups using paired samples t tests. In instances where the assumption of normality was not met (based on the Kolmogorov–Smirnov test), the nonparametric Mann–Whitney U test was applied instead. A P value < 0.05 was considered statistically significant.

Results

Our study initially enrolled 90 patients who were then randomly assigned into one of 3 groups (n = 30 per group). All 90 patients were included in the final analysis. The mean (SD) age of was 39.5 (5.8) years. There were 50 (55.6%) women and 40 (44.4%) men. There were no significant differences among the 3 groups in terms of age, gender distribution, or other baseline characteristics (Table 1).

In all three groups, VAS and SSS scores showed statistically significant decreases from baseline to month 3 (P = 0.04 and P = 0.03, respectively), and from month 3 to month 6 (P < 0.05 for both). However, in the hypertonic saline and hyaluronidase groups, there was no statistically significant difference between month 6 and month 12 (P = 0.267 and P = 0.071 for the hypertonic saline group; P = 0.13 and P = 0.10 for the hyaluronidase group, respectively).

In our study, the VAS and SSS scores in the hyaluronidase group showed a statistically significant reduction compared to both the normal saline and hypertonic groups at postinjection months 3, 6, and 12 despite the normal saline and hypertonic groups receiving more injections (Tables 2–5). Postinjection satisfaction levels had a statistically significant increase in all 3 groups (P = 0.001 in all 3 groups). Satisfaction in the hyaluronidase group showed a significant increase compared to both the normal saline and hypertonic groups at postinjection months 3, 6, and 12 despite the normal saline and hypertonic saline groups receiving more injections (Tables 3,6).

The number of injections needed in the hyaluronidase group was significantly lower compared to the other 2 groups (P = 0.001 for both) whereas the hypertonic group did not show a statistically significant difference compared to the normal saline group (P = 0.8) (Table 3).

The number of injections needed, satisfaction levels, SSS scores, and VAS scores in the hypertonic group did not have a statistically significant difference compared to the normal saline group at postinjection months 3, 6, and 12 (Tables 3-6).

Discussion

Our study aimed to compare the efficacy of hyaluronidase hydrodissection with other treatments for postoperative relapse of carpal tunnel syndrome; this relapse occurs in 10%–25% of patients (19). Our findings show that hyaluronidase provides superior long-term outcomes, supporting its use as an effective treatment option. Our results show that patients in the hyaluronidase hydrodissection group had a statistically significant improvement in pain and symptom severity scores and patient satisfaction level compared to patients in the normal saline and hypertonic saline groups at postinjection month 12.

Table 1. *Study patient demographics.*

Group Variable	Normal Saline	Hypertonic Saline	Hyaluronidase	*P* value
Age	38.3 (6.1)	39.5 (5.9)	41 (4.5)	0.2
Gender (women/men)	16/14	18/12	16/14	0.6
Height, cm	167 (6.98)	166.6 (6.9)	165.8 (6.96)	0.54
Weight, kg	83.2 (11.67)	84.2 (10.2)	85.88 (9.47)	0.44
Body Mass Index (kg/m^2)	29.8 (2.69)	30.3 (2.7)	31.2 (2.95)	0.07

Values are presented as mean (SD). $P < 0.05$ is significant.

Table 2. *Follow-up of patients with a Visual Analog Scale pain score < 4.*

Time frame Groups	3 Months	6 Months	12 Months
Normal saline	19	16	26
Hypertonic saline	23	19	26
Hyaluronidase	28	29	29

The number of patients whose level of pain, based on VAS score from zero to 4, is specified within the defined time interval.

Table 3. *Number of patients who had a repeat injection.*

Number of injections needed Groups	1 injection	2 injections	3 injections
Normal saline	8	18	4
Hypertonic saline	10	15	5
Hyaluronidase	26	3	1

We found considerable improvement in the SSS and VAS scores as well as patient satisfaction levels in both the normal saline and hypertonic saline groups after each injection. There was no statistically significant difference between these 2 groups in these outcomes, indicating a comparable therapeutic effect. This suggests that nerve liberation through hydrodissection is effective regardless of whether a normal saline or hypertonic saline solution is used.

The results of our study align with the findings reported by Yeo, et al (37) regarding the effectiveness of hyaluronidase injections for reducing pain. While this study showed a statistically significant reduction in postinjection VAS scores in the hyaluronidase group compared to preinjection scores (mean change 1.42, $P = 0.030$), our results showed a more pronounced and sustained improvement. In our study, the hyaluronidase group showed a mean VAS reduction from 5.1 at preinjection to 2.5 at postinjection month 3 and further to 1.7 at postinjection month 12, compared to smaller reductions in the normal saline and hypertonic saline groups. This suggests that hyaluronidase injections applied by fellowship-trained practitioners may provide superior and more durable pain relief compared to other injection methods. Additionally, the observed long-term effectiveness in our study further highlights the potential benefits of hyaluronidase, particularly in achieving sustained pain relief beyond the immediate postinjection period (37).

By comparing the Alsaeid, et al study's results (38) with our results, it is evident that both studies highlight the short-term and long-term effectiveness of hyaluronidase injections for symptom severity and functional improvement. In the Alsaeid, et al study (38), the hyaluronidase group showed a significant reduction in SSS scores from a preinjection value of 31, to a value of 14.9 at 6 months, with sustained improvement up to 6 months compared to the normal saline group, which showed a return to near preinjection levels. Similarly, our results reveal that hyaluronidase injections reduced the mean SSS score from 29.9 to 19.8 at postinjection month 3 and further to 14.8 at postinjection month 6. While the hypertonic group in our study also showed substantial improvement (mean SSS score reduced from 29.6 to 17.8), the normal saline group had a more limited effect, with their mean SSS score decreasing from 28.8 to 19.6. Our findings, along with Alsaeid, et al's findings (38), underscore the superior and sustained efficacy of hyaluronidase injections compared to normal saline or hypertonic saline solutions, particularly over longer durations, supporting their role as an effective therapeutic intervention when administered by trained practitioners.

The exact pathophysiology of CTS is not understood. Proposed mechanisms include increased pressure within the carpal tunnel due to fibrosis of connective tissue, swelling within the tunnel, and adhesion of flexor tendon synovial connective tissue around the median nerve. Hydrodissection may alleviate these adhesions, thereby freeing the nerve from surrounding tissues (1,39).

Kremer, et al (40) examined the efficacy of local steroid injection in a similar patient population and found that while initially effective for symptom relief compared to placebo, the difference diminished over a 5-year follow-up period. Nonetheless, steroid injection appeared to delay the need for surgery and provided sustained symptom relief in some cases.

Table 4. *Visual Analog Scale pain scores at baseline (preinjection) and follow-ups.*

Variables	Normal Saline Group vs Hyaluronidase Group			Normal Saline Group vs Hypertonic Saline Group			Hypertonic Saline Group VS Hyaluronidase Group		
	Normal Saline Group	Hyaluronidase Group	*P* Value	Normal Saline Group	Hypertonic Saline Group	*P* Value	Hypertonic Saline Group	Hyaluronidase Group	*P* Value
Preinjection	5.6 (0.9) (4–7)	5.1 (0.9) (4–7)	0.055	5.6 (0.9) (4–7)	5.5 (1.0) (4–7)	0.7	5.5 (1.0) (4–7)	5.1 (0.9) (4–7)	0.122
Month 3 Follow-up	3.8 (1.6) (1–7)	2.5 (0.1) (1–5)	0.001	3.8 (1.6) (1–7)	3.3 (1.1) (2–6)	0.2	3.3 (1.1) (2–6)	2.5 (0.1) (1–5)	0.003
Month 6 Follow-up	3.3 (1.1) (1–5)	2.2 (1.0) (1–5)	0.001	3.3 (1.1) (1–5)	3.1 (1.0) (1–5)	0.25	3.1 (1.0) (1–5)	2.2 (1.0) (1–5)	0.002
Month 12 Follow-up	2.9 (0.8) (1–5)	1.7 (0.9) (1–4)	0.001	2.9 (0.8) (1–5)	2.6 (0.9) (1–4)	0.09	2.6 (0.9) (1–4)	1.7 (0.9) (1–4)	0.001

Values are presented as mean (SD) and range. $P < 0.05$ is significant.

Table 5. *Symptom Severity Scale scores at baseline (preinjection) and follow-ups.*

Variables	Normal Saline Group vs Hyaluronidase Group			Normal Saline Group vs Hypertonic Saline Group			Hypertonic Saline Group vs Hyaluronidase Group		
	Normal Saline Group	Hyaluronidase Group	*P* Value	Normal Saline Group	Hypertonic Saline Group	*P* Value	Hypertonic Saline Group	Hyaluronidase Group	*P* Value
Preinjection	28.8 (5.2)	29.9 (4.5)	0.10	28.8 (5.2)	29.6 (4.8)	0.20	29.6 (4.8)	29.9 (4.5)	0.10
Month 3 Follow-up	26.4 (3.1)	19.8 (3.5)	0.001	26.4 (3.1)	24.4 (2.8)	0.15	24.4 (2.8)	19.8 (3.5)	0.003
Month 6 Follow-up	22.4 (3.8)	15.9 (3.5)	0.001	22.4 (3.8)	21.6 (3.4)	0.17	21.6 (3.4)	15.9 (3.5)	0.002
Month 12 Follow-up	19.6 (3.5)	14.8 (3.3)	0.001	19.6 (3.5)	17.8 (3.9)	0.11	17.8 (3.9)	14.8 (3.3)	0.001

Values are presented as mean (SD). $P < 0.05$ is significant.

Table 6. *Patient satisfaction with their injections.*

	Normal Saline Group vs Hyaluronidase Group			Normal Saline Group vs Hypertonic Saline Group			Hypertonic Saline Group vs Hyaluronidase Group		
Variables	Normal Saline Group	Hyaluronidase Group	*P* Value	Normal Saline Group	Hypertonic Saline Group	*P* Value	Hypertonic Saline Group	Hyaluronidase Group	*P* Value
Month 3 Follow-up	26.7%	93%	0.001	26.7%	46.7%	0.111	46.7%	93%	0.001
Month 6 Follow-up	60%	90%	0.008	60%	66.7%	0.595	66.7%	90%	0.03
Month 12 Follow-up	66%	96%	0.003	66%	76.7%	0.394	76.7%	96%	0.024

Each column displays the percentage of patients who had acceptable satisfaction.

Comparing the findings of the Peters-Veluthamaningal, et al study (41) evaluating steroid injections for CTS with our own investigation on hyaluronidase injections, several notable distinctions and parallels emerge. Both studies underscore the significance of short-term efficacy for symptom management. While the steroid injections showed substantial short-term effects in symptom alleviation, as evidenced by statistically significant improvements in symptom severity and functional status, our study showed a similar trend with hyaluronidase injections. Specifically, hyaluronidase injections led to considerable improvement in pain severity and satisfaction, outperforming normal saline and hypertonic saline solutions. Additionally, both studies

acknowledge the challenge of sustaining long-term effectiveness. In the steroid study, despite initial positive responses, over a 12-month follow-up period scores for symptom severity and functional status deteriorated, with a notable recurrence rate necessitating further interventions (41). Similarly, our investigation showed that while hyaluronidase injections yielded superior long-term outcomes compared to normal saline and hypertonic saline solutions, sustained effectiveness remains a concern. However, the notable advantage of hyaluronidase injections lies in their ability to sustain lower pain severity levels over time, suggesting a potential for prolonged symptom relief compared to alternative treatments. Thus, while each study offers valuable insights into treatment efficacy and sustainability for CTS, our findings underscore the promising potential of hyaluronidase injections in addressing both short-term symptom management and long-term outcomes.

Limitations

Our study has several limitations. First, all 3 intervention groups included methylprednisolone in the injection mixture, which may have confounded the isolated effects of hyaluronidase, hypertonic saline, and normal saline. Future studies should consider using hyaluronidase as a standalone agent to better evaluate its independent efficacy in hydrodissection therapy. Second, the study was conducted in a single center, which may limit the generalizability of the findings to broader populations or health care settings. Third, advanced imaging or electrophysiological tools were not used to objectively assess anatomical or functional nerve changes following treatment. Third, our study was limited to a postinjection 12-month follow-up; longer-term outcomes remain to be explored in future research. Finally, higher loss to follow-up in the normal saline and hypertonic saline groups at postinjection months 3 and 6 compared to the hyaluronidase group may have confounded the results at these time points.

Conclusion

Our study shows that median nerve hydrodissection with hyaluronidase, serving as an adhesiolysis agent, resulted in significantly greater improvements in pain severity, functionality, and patient satisfaction at postinjection months 3, 6,and 12 compared to the other groups. While all treatment groups had improvement in pain and function throughout the study, particularly in VAS scores and satisfaction, the hyaluronidase group showed superior outcomes, indicating that hydrodissection with hyaluronidase is more effective. However, the observed improvements in patients receiving normal saline or hypertonic saline also suggest that nerve liberation through hydrodissection alone, regardless of the solution used, offers beneficial effects for CTS management.

Author Contributions

MS, conceptualization, methodology, supervision; AAD, conceptualization, methodology, supervision; HM, conceptualization, methodology, supervision; AA, writing—review and editing, investigation, review of final submission; YY, formal analysis, writing—review and editing; MC, writing—review and editing, investigation, review of final submission. All authors reviewed and approved the final submission.

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