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Review article

A systematic review and meta-analysis of the effectiveness of perineural dextrose injection in peripheral compression neuropathies of the upper limbs

Fatemeh Azizi [a], Faezeh Saber Gharesoo [a,b], Fereshteh Eidy [a], Sama Heidari [c], Nastaran Maghbouli [a,c,*], Shirin Djalalinia [d,**], Amir Kasaeian [e,f,g]

[a] Center for Orthopedic Trans-Disciplinary Applied Research, Tehran University of Medical Sciences, Tehran, Iran
[b] Student Research Committee, Faculty of Medicine, North Khorasan University of Medical Sciences, Bojnurd, Iran
[c] Department of Physical Medicine and Rehabilitation, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[d] Research and Technology, Ministry of Health and Medical Education, Tehran, Iran
[e] Digestive Oncology Research Center, Digestive Disease Institute, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran
[f] Research Center for Chronic Inflammatory Diseases, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran
[g] Clinical Research Development Unit, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran

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ABSTRACT

Background: Entrapment neuropathies, marked by nerve compression at various anatomical sites, can be effectively managed using conservative approaches like injections. Dextrose 5 % water injection has emerged as a potential therapy by reducing inflammation and promoting tissue regeneration. We aimed to evaluate dextrose injection's efficacy in treating entrapment neuropathies in upper extremities.

Method: We systematically searched EMBASE, Scopus, Web of Science, and PubMed. Our eligibility criteria included participants aged 18 and older who had peripheral upper limb nerve entrapment from non-metabolic and non-traumatic sources. These participants were treated with dextrose injection compared to those receiving other injectables, such as corticosteroids and non-corticosteroid medications. The primary outcome was pain, with secondary outcomes including function, ultrasonographic, and electrodiagnostic findings. The quality of the clinical trials was assessed using Cochrane tools. Random-effect model was employed for meta-analysis.

Results: Thirteen studies, involving 784 patients, were included, with only two showing serious bias risk. Initial findings indicate significant pain relief with dextrose injection within a short time (≤4 weeks) compared to normal saline (MD: −1.30, 95%CI: −2.13; −0.47). Dextrose also demonstrated a significant pain decrease compared to corticosteroids (MD: −0.81, 95 % CI: −1.40; −0.22) with low heterogeneity (I^2 = 8 %, P = 0.36), and significantly improved function (MD = −0.46, 95 % CI −0.78; −0.14) with low heterogeneity (I^2 = 17 %, P = 0.31) in mid-term (one to six months).

Conclusion: This meta-analysis suggests dextrose injection as an effective therapy for managing pain and restoring function in entrapment neuropathies. However, further high-quality studies are needed to confirm these findings and establish optimal dosing regimens and injection

* Corresponding author. School of Medicine, Tehran University of Medical Sciences, Poursina Ave, Tehran, Iran.
** Corresponding author. Ministry of Health, Treatment and Medical Education, Sima-ye-Iran St, Shahrak Gharb, 1467664961, Tehran, Iran.
E-mail addresses: [illegible] (N. Maghbouli), [illegible] (S. Djalalinia).

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protocols. Healthcare providers should consider integrating dextrose injection into their treatment strategies for patients with entrapment neuropathies.

1. Introduction

Entrapment neuropathies (ENP) are the result of nerve compressions along various anatomical structures caused by exogenous factors such as foreign bodies and orthopedic implants, as well as endogenous ones, including tumors, bony spurs, and thickened connective tissue [1]. ENPs, including carpal tunnel syndrome (CTS) and ulnar neuropathy at the elbow (UNE) as the most common types, play a significant role in upper limb disabilities [2]. Despite their high prevalence, their pathogenesis is still unclear, but generally, ischemia and nerve swelling at the site of entrapment impair neural conduction and result in neuropraxia or axonotmesis [3]. ENPs give rise to diverse clinical presentations, such as mild discomfort, numbness, tingling, pain, burning sensation, muscular weakness, or paralysis [4]. Depending on the severity, management could be conservative or surgical. Mild to moderate neuropathy management includes night splints, nonsteroidal anti-inflammatory drugs (NSAIDs), physical therapy, and activity modification [5]. In light of a Cochrane review on CTS, developing new approaches for conservative management is crucial due to the limited long-term efficacy of the mentioned conservative treatments [6]. Perineural Injection Therapy (PIT), which was conceptualized as injection, is a popular method for treating peripheral nerve entrapments [7]. Given the possible adverse effects of corticosteroids, including skin thinning, tendon rupture, soft tissue atrophy, and crystal-induced synovitis [8,9], there is a need for alternative injectants. "Lidhagi" introduced perineural injection using dextrose to reduce neurogenic inflammation by inhibiting capsaicin-sensitive receptors. This inhibition suppresses substance P and calcitonin gene-related peptide secretion, both of which cause pain and inflammation in the nerves and surrounding tissues [10]. "Wu" et al. found glucose semiconductor effectors in inhibiting TNF-α-induced NF-κB, proinflammatory cytokine upregulation, and metabolic dysfunction, all of which are responsible for neuroinflammation [11]. "Li" et al. suggested a possible unknown nerve regenerative process responsible for the lasting effects rather than dextrose's anti-inflammatory and hydro-dissection effects [12]. Although this hypothesis remains unconfirmed, a study by "Hansen" et al. suggested that glucose may potentially regenerate nerves [13]. Looking for the healing mechanisms of perineural dextrose injection for nerve entrapment, "Shu" et al. found that in early responses to hyperglycemia, Schwann cells (SCs) increase the expression of neurotrophic factors (NTF), and high glucose levels also increase the expression of nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF) induced by p42/p44 MAPK activation [14]. These findings suggest glucose's possible dose-related neuro-regenerative potential, which requires further in vivo and in vitro studies. Additionally, no harmful effects have been reported from animal and human studies on dextrose [15,16].

A recent network meta-analysis approved the effectiveness of dextrose perineural injection among CTS patients in comparison to placebo, while PRP was better than dextrose and steroids considering pain and function improvement [17]. However, their review focused only on CTS and the short-term effectiveness of injections. Another systematic review and network meta-analysis in 2020, on ten studies, sought DSW (dextrose 5 % water), PRP (platelet-rich plasma), corticosteroids, normal saline, and splinting effects on CTS. They found DSW to be the most effective and PRP to be second-ranked for symptom relief and splinting for better functional outcomes [18]. Furthermore, existing meta-analyses do not pool the results of limited randomized clinical trials that evaluated the effectiveness of dextrose PIT in UNE [19,20].

In summary, the effectiveness of the recently used DSW injectate remains controversial among the available evidence, especially for different types of peripheral nerve entrapments and various outcome measures, including clinical, sonographic, and sonographic findings. Given the aforementioned gap, this study aimed to assess the efficacy of dextrose PIT for upper limb entrapment neuropathies and compare it with other injectants.

2. Methods

We used "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" (PRISMA) guidelines [21] to perform this study. The protocol has been registered in PROSPERO, assigned the registration number CRD42023407106.

2.1. Data sources and search strategies

We conducted systematic searches in EMBASE, Scopus, Web of Science, and PubMed without any language or study design restrictions from their inception until July 8, 2023. We utilized Medical Subject Headings (MeSH) and Emtree when appropriate. The search strategy was developed based on the main axis of: "entrapped neuropathy," "nerve compression syndrome," "nerve entrapment," "carpal tunnel syndrome," "ulnar nerve entrapment," "median nerve entrapment," "radial nerve entrapment," for the population, and "dextrose," and "DSW" for the intervention, which were combined using "AND" Boolean. Between each phrase of the same category, the "OR" Boolean was used. The query did not include the comparator and outcomes to avoid narrowing down the search results. Additionally, we conducted manual searches of the reference lists of all the included studies and existing review articles to ensure that we did not miss any studies. If it was necessary to access more specific data, we emailed the corresponding authors of some studies (Please look for the supplementary file of the precise search queries).

Table 1
Summary of studies' characteristics and findings.

Author, year	Design	Nerve entrapment	Injectate	Sample size (intervention, control)	Age (intervention, control) (years, mean, SD)	Gender (intervention, control) (M/F)	Number of sessions	Outcome measures	Follow-up	Rescue/other treatments	Side effects and adjuvant treatments
"Wu" et al., 2017	RCT	CTS	Dextrose vs. NS	[illegible] (30, 30)	I:56.47 ± 2.22 C:58.10 ± 1.82	I: 4/26 C: 6/24	Single session	VAS BCTQ CSA SNCV Physician global assessment	3 and 6 months	–	[illegible]
"Wu" et al., 2018	RCT	CTS	Dextrose vs Corticosteroid (Triamcinolone acetonide)	54 (27, 27)	I:56.0 ± 2.2 C: 54.2 ± 2.0	I: 3/22 C: 0/21	Single session	VAS BCTQ CSA DML	1, 3, 4, and 6 months	–	[illegible]
"Shen" et al., 2019	RCT	CTS	Dextrose vs. PRP	52 (26, 26)	I:58.8 ± 2.1 C: 55.8 ± 1.7	I: 4/22 C: 1/25	Single session	BCTQ CSA DML SNCV	1, 3 and 6 months	–	[illegible]
"Li" et al., 2020	observational	CTS	Dextrose	188	55.4	64/121	Single session	CSA SNCV DML	1–3 years	Acupuncture, physical modality, analgesic agents, surgery	None- not mentioned
"Chen" et al., 2020	RCT	Ulnar neuropathy	Dextrose vs. Corticosteroid (Triamcinolone acetonide)	28 (17, 16)	I:55.5 ± 2.2 C:58.5 ± 2.3	I: 5/12 C: 6/10	Single session	VAS DASH SNCV CSA physician's global assessment	1, 3, 4 and 6 months	–	Not reported- [illegible]
"Lin" et al., 2022	RCT	CTS	Dextrose (1, 2 and 4 mL)	45 (G1: 17 G2: 14 G3: 14)	G1:56.8 ± 8.1 G2:52.8 ± 10.2 G3:58.2 ± 8.2	G1: F:94.1 % G2: F:85.7 % G3: F:85.7 %	Single session	VAS BCTQ CSA Mobility Shear-wave elastography	1st, 4th, 12th and 24th week		Not reported- [illegible]
"Ho" et al., 2022	retrospective	CTS	Dextrose	32	58.2 ± 1.7	6/48	Single session	SNCV DML CSA VAS BCTQ	6 months	–	Not reported- [illegible]
"Aghaei" et al., 2022	RCT	CTS	Dextrose vs Corticosteroid (Triamcinolone acetonide)	40 (20, 20)	I:51.5 ± 6.7 C:48.8 ± 9.2	I:3/17 C:3/17	Single session	BCTQ VAS [illegible] DML SNAP CMAP	1, 3 and 12 months	Surgery, re-injection	pain, swelling, and heaviness sensation after injection, [illegible]
"Babaei-Ghazani" et al., 2022	RCT	CTS	Dextrose vs. Corticosteroid	54 (27, 27)	I:48.40 ± 11.88 C:49.28 ± 8.75	–	Single session	VAS CSA	2, 6, 12 weeks	–	None- [illegible]

(continued on next page)

Table 1 (continued)

Author, year	Design	Nerve entrapment	Injectate	Sample size (intervention, control)	Age (intervention, control) (years, mean, SD)	Gender (intervention, control) (M/F)	Number of sessions	Outcome measure	Follow-up	Rehabilitation/ Treatment	Side effects and adjuvant treatments
			(Triamcinolone acetonide)					DN4 DSS BCTQ SNCV CMAP EQ5D	and 6 months		
"Chen" et al., 2021	retrospective	CTS	Dextrose	38	58.2 ± 1.6	8/30	2.1 ± 0.8 At 1–4 weeks interval	CSA VAS	6–87 months	progression, rehabilitation, and medication	Not reported.
"Bagheri" et al., 2022	RCT	Ulnar neuropathy	Dextrose vs. NS	46 (23, 23)	I:43.6 ± 13.8 C:38.1 ± 13.7	I:9/14 C:9/14	2 sessions at 2 weeks intervals	VAS Q-DASH CSA SNCV NCV latency	2, 4 and 12 weeks	–	None- reported.
"Wu" et al., 2021	retrospective	CTS	Dextrose vs. NS, PRP, and HA	52 (13, G1: 13, G2: 13, G3: 13)	I: 54.2 ± 1.3 C- G1: 54.9 ± 1.2 G2: 54.8 ± 1.2 G3: 54.1 ± 1.2	I:7/6 C- G1:7/6 G2:7/6 G3:7/6	Single session	BCTQ CSA	1 and 6 months	–	Non- physiotherapy, splints, Pentoxifylline, gabapentin, vitamin B and E
"Hasti" et al., 2020	RCT	CTS	Dextrose vs. Corticosteroid (Methylprednisolone)	38 (21, 22)	I: 46 C: 47.3	I:7/14 C:4/17	Single session	VAS BCTQ-SS BCTQ-F CSA	3 months	–	Severe pain, discomfort and fatigue after injection- Splint, lifestyle modification, energy conservation techniques

2.2. Data extraction and inclusion and exclusion criteria

The inclusion criteria were: 1. Population: involvement of human participants aged 18 and above with entrapment neuropathy in the upper limbs; 2. Outcomes: studies reporting outcomes related to pain, function, nerve conduction studies, or ultrasonographic findings; and 3. Comparators: the presence of control groups involving perineural injections such as normal saline, local anesthetics, platelet-rich plasma (PRP), corticosteroids; 4. Intervention: using dextrose PIT. 5. Clinical trials and experimental studies with control groups. Exclusion criteria were: 1. articles such as comments, expert opinions, case reports, case series, conference meeting abstracts, surveys, reviews, editorials, systematic reviews, meta-analyses, observational studies, and letters; 2. neuropathies resulting from metabolic causes (such as diabetes), hereditary factors, trauma, or surgical procedures; and 3. studies lacking data in the form of means

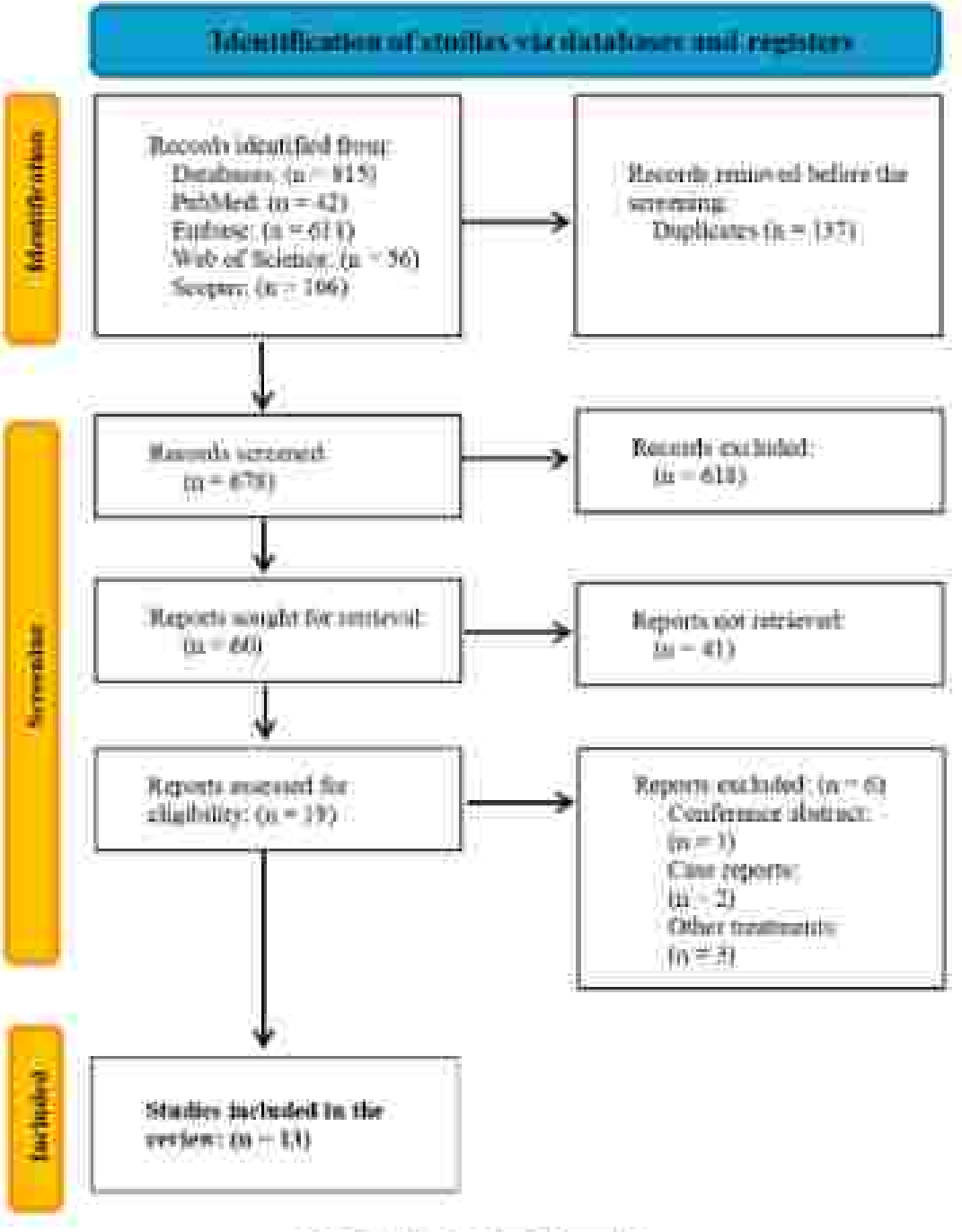

Fig. 1. PRISMA flow diagram of screening.

and IDs are successively excluded due to limitations for analysis.

Two reviewers (F.J. and S.H.) independently screened the articles based on the title and abstract and the studies eligible for full-text screening. Although most studies were about Median and Ulnar nerve entrapment, we found no available studies on various types of radial nerve entrapments treated by decompression during studies screening. Still, all were single-case injection case reports, and their sample sizes of one or two cases were inadequate to drive conclusions. Therefore, radial nerve entrapment studies were not included. The same authors extracted the information from the included studies in a prepared Excel sheet, including the author, year, study design, sample size, patients' demographic data, symptoms duration, intervention characteristics, follow-up sessions, the usage of ultrasound guidance for injection and reported outcomes such as visual analog scale for pain (VAS), Boston questionnaires for function and pain (BCTQ-FS and BCTQ-SS), ultrasonographic findings (cross-sectional area (CSA)), nerve conduction studies (distal motor latency (DML), distal sensory latency (DSL), sensory nerve action potentials (SNAP), compound muscle action potentials (CMAP), sensory nerve conduction velocity (SNCV), and motor nerve conduction velocity (MNCV)).

2.2. Outcome measures

The primary interested outcome was pain assessment using the Visual Analog Scale (VAS) [24]. Secondary outcomes included the cross-sectional area (CSA) of the nerve in ultrasonography and the Boston Carpal Tunnel Questionnaire (BCTQ), which has two separate parts: the symptom severity scale (SSS) and the functional status scale (FSS). Electrophysiological variables, such as sensory nerve conduction velocity (SNCV) and distal motor latency (DML), were also considered secondary outcomes. Additionally, adverse effects were extracted.

2.4. Quality assessment

We used Cochrane-approved tools to evaluate the risk of bias in the included studies [25,26]. We used ROB2 [27] for randomized trials and ROBINS-I [28] for non-randomized studies. Two independent assessors (S.H. and F.J.) evaluated the studies. In cases of disagreements, a third party (F.A.) made the final decision to resolve conflicts. These tools focused on trial design, study conduct, and reporting aspects. By answering the signaling questions in each domain, the risk of bias was classified as 'Low,' 'High,' or with 'Some concerns' for ROB 2 and "Low," "Moderate," "Serious," and "Critical" for ROBINS-I. The plots were visualized using the Risk-of-Bias Visualization tool (Robvis) [29].

2.5. Statistical analysis

We performed the statistical analysis using the R Meta package, version 4.3.1. Radial plots were employed for more than three studies to identify outliers, and a random-effects model was implemented. The variable follow-ups of the studies were pooled as "short-term" for equal and less than 4 weeks, "medium-term" for 4–24 weeks, and "long-term" for more than 6 months. The study by Wu [30] had three control arms, and each was considered an independent data set for analysis. We utilized mean and standardized mean differences to compare the means between the intervention and control groups. We employed Cochran's Q test and the I2 statistic to assess between-study heterogeneity. We attempted to reduce heterogeneity by subgroup analysis (based on the follow-up times and the type of injections) and sensitivity analysis. We tried to do meta-regression using variables like age and pain duration. Unfortunately, the mentioned data was reported in less than ten studies, making meta-regression analysis impossible. Finally, we used Egger's and Begg's tests to identify potential publication bias.

3. Results

3.1. Study characteristics

The final investigations included 13 studies involving a total of 734 patients. 185 patients were male, and 515 were female, respectively (except for one study that did not report the genders). Pathologic nerves were ulnar in two studies, and the rest were

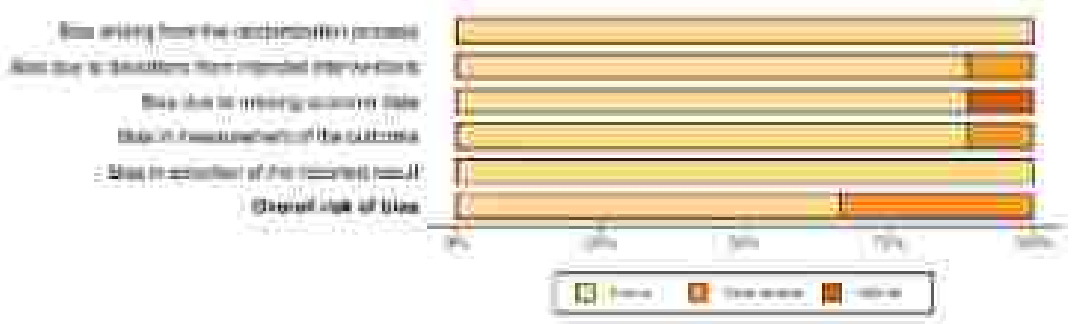

Fig. 2. ROB 2, a revised tool to assess risk of bias in randomized trials.

Fig. 3. ROBINS-I, risk of bias in non-randomized studies - of interventions.

Table 2
Meta-analysis findings of dextrose prolotherapy injection effectiveness considering different outcomes.

Outcome	No. of included studies	Subgroup	Pooled WMD	95 % CI	I^2	P value for I^2
VAS (short-time)	5	Total	−0.18	−0.67, 0.30	20	0.29
	3	Corticosteroids	−0.18	−0.38, 0.06	0	0.40
	2	Non-corticosteroids	−1.3	−2.13, −0.47	16	0.27
VAS (medium-time)	5	Total	−1.05	−1.68, −0.42	38	0.18
	3	Corticosteroids	−0.81	−1.40, −0.21	5	0.36
	2	Non-corticosteroids	−3.21	−7.27, 0.34	90	<0.01
SPADI (short-time)	3	Total	0.64	−0.04, 1.32	78	0.01
SPADI (medium-time)	3	Total	1.22	0.30, 2.14	88	<0.01
SDQ (short-time)	4	Total	−0.03	−0.84, 0.78	0	0.98
	2	Corticosteroids	0.20	−1.03, 1.40	0	0.98
	2	Non-corticosteroids	−0.22	−1.38, 0.81	0	0.89
SDQ (medium-time)	3	Total	−0.09	−0.26, 0.08	81	0.04
	3	Corticosteroids	−0.02	−0.26, 0.23	72	0.03
	2	Non-corticosteroids	−0.17	−0.44, 0.10	18	0.28
CSA (short-time)	7	Total	0.37	0.01, 0.73	0	0.64
	4	Corticosteroids	0.38	−0.05, 0.78	0	0.78
	4	Non-corticosteroids	0.09	−0.67, 0.80	42	0.16
CSA (medium-time)	7	Total	0.46	−0.01, 0.93	52	0.04
	4	Corticosteroids	0.31	−0.67, 0.24	0	0.46
	4	Non-corticosteroids	0.14	−2.54, 2.28	68	0.02
ROM_AB (short-time)	5	Total	0.07	−0.21, 0.35	0	0.72
	3	Corticosteroids	0.10	−0.24, 0.44	0	0.45
	2	Non-corticosteroids	−0.22	−1.30, 0.87	82	0.07
ROM_AB (medium-time)	5	Total	−0.28	−0.76, 0.09	46	0.14
	2	Corticosteroids	−0.24	−0.72, 0.24	27	0.27
	2	Non-corticosteroids	−0.47	−1.16, 0.22	83	0.07
ROM_ER (short-time)	7	Total	−0.48	−0.82, −0.14	50	0.08
	3	Corticosteroids	0.02	−0.31, 0.36	0	0.84
	4	Non-corticosteroids	−1.11	−1.73, −0.48	72	0.01
ROM_ER (medium-time)	8	Total	−0.46	−0.76, −0.16	17	0.31
	3	Corticosteroids	−0.42	−0.87, 0.02	0	0.79
	4	Non-corticosteroids	−0.88	−1.65, −0.08	80	<0.01

median. One study was conducted in Turkey, three in Iran, and nine in Taiwan (Republic of China). Four of them were retrospective, and the others were randomized controlled trials. These studies' publication dates ranged from 2017 to 2023. Of the four retrospective studies, three had no control groups and were not included in the meta-analysis [12,27,28]; the other one was "Wu" et al.'s [21] study with three control groups, which was included in the meta-analysis. Eight two-arm randomized controlled trials looked at how well dextrose injection worked compared to corticosteroids (triamcinolone acetonide [29–32] and methylprednisolone [33]) and non-corticosteroids (PRP [26, 33], normal saline 0.9 % [19, 25, 34], and hyaluronic acid [26]) (Table 1) (see Fig. 1).

3.2. Risk of bias

Based on ROB-2, three studies had some concerns [14,26,31], and the rest were low on bias. In the study by "Sobieni" et al. [32], the baseline information and all outcomes were assessed by the same physician. The study by Manzo-Kaplan [14] had missing outcome data for seven patients, and they were excluded from the study without detailed information. In the study by "Shen" et al. [33], participants were not blinded to their choice of treatment. None of the studies in ROBINS-I had a low risk of bias. Three [13,27,28] had a moderate risk of bias due to the potential confounding effect on the interventions regarding their retrospective design. Five [14,29] had moderate risk in domain two due to a notable time interval between the intervention and the first follow-up. Two studies [12,31] had a moderate risk of bias in domain five due to a considerable number of missing participants' outcome data. Considering the outcome assessors' awareness of the participants' intervention, nine [26,27] studies exhibited a moderate risk of bias in domain 6, while two [13,28] faced a serious risk due to the same cause and an inadequate qualitative outcome report (Figs. 3 and 4) (see Table 2).

3.3. Short-term VAS

Seven studies were eligible for random-effects model meta-analysis. Two of them had close monograph [13,14], and the rest had CTS [26–32]. Five of them were comparing dexmex with normal saline [26,34] and others with corticosteroids [29–32]. The Galbraith plot identified two studies [13,34] as outliers, leading to their removal from the analysis. Of the remaining five studies, there were no significant differences between the experimental and control groups regarding the reduction of pain (MD: −0.18, 95 % CI: −0.47; 0.10), with low heterogeneity (I^2 = 22 %, p = 0.28). The result of Egger's test for possible meta-bias was insignificant (P > 0.49) (Table 3 & Supplementary).

3.4. Subgroup of short-term VAS

The meta-analysis of five studies of dexmex versus corticosteroid [14,26,29–32] revealed no difference between the two injections (MD: 0.16, 95 % CI: −0.35; 0.68), but compared with two studies of NS [13,34], dexmex injection was significantly superior in pain relief (MD: −1.30, 95 % CI: −2.12; −0.47). Also, it was notable that this decrease was more visible for close monograph [14] compared with the study of CTS [34] (MD: −2.3 and −1.15, respectively). Both subgroups had low heterogeneity (I^2 = 0 and 14 % for corticosteroid and N/S controls, respectively).

3.5. Mid-term VAS

Based on the Galbraith plot, we dropped the study by Manzo-Kaplan [14] and performed the analysis on the rest. Results showed a significant difference between groups favoring dexmex injection (MD: −1.02, 95 % CI: −1.62; −0.43), with nonsignificant heterogeneity (I^2 = 38 %, P = 0.15). Egger's test revealed no meta-bias (P = 0.78).

3.6. Subgroup of mid-term VAS

We found a significant decrease in pain for dexmex compared with the corticosteroid group (MD: −0.81, 95 % CI: −1.40; −0.21) with low heterogeneity (I^2 = 0 %, P = 0.36). For dexmex versus NS, we found no statistical difference between the groups in decreasing pain (MD: −3.68, 95 % CI: −7.37; 0.34) with a significantly high heterogeneity (I^2 = 80 %, P < 0.01).

3.7. Short-term SNCV

This variable was comparable among three studies, comparing dexmex injection to NS [34], corticosteroid [31], and PRP [33]. There was no significant difference between the efficacy of dexmex and other treatments in the control group (MD: 0.64, 95 % CI: −0.64; 1.92) with high and significant heterogeneity (I^2 = 78 %, p = 0.01). The Egger test revealed no publication bias (P = 0.70).

3.8. Mid-term SNCV

There was also no statistically significant difference between dexmex and other treatments in improving the SNCV score over a medium period of time (MD: 1.32, 95 % CI: −0.49; 3.14). A high heterogeneity was detected with statistical significance (I^2 = 86 %, p < 0.01). The meta-bias was insignificant (P = 0.39).

3.9. Short-term DASI

Four studies [27,31,32,34] were eligible for random-effect model meta-analysis. Two studies used corticosteroids [26,31] as the control group, while one others injected NS [34] and PRP [33]. No difference was found between the experimental and control groups (MD: 0.05, 95 % CI: −0.84; 0.73) without heterogeneity (I^2 = 0 %, p = 0.96). The Egger test's findings showed no evidence of publication bias (p = 0.66). Omitting each study for sensitivity analysis did not affect the results, demonstrating the robustness of pooled estimates.

3.10. Subgroups of short-time DME

Both subgroups of the corticosteroid and non-corticosteroid control groups (MD: 0.20, 95 % CI: −1.02, 1.42; and MD: −0.23, 95 % CI: −1.28, 0.81, respectively) showed no significant differences, and there was no heterogeneity (I^2 = 0 %, P = 0.96, and I^2 = 0 %, P = 0.89).

3.11. Mid-time DME

Five studies with corticosteroids [28–31], NS [34], and PRP [32] as control groups were included. The analysis revealed no difference between dextrose and all other controls (MD: −0.09, 95%CI: −0.26, 0.08). The heterogeneity was significant (I^2 = 61 %, P = 0.04). The Egger test for publication bias was insignificant (p = 0.16). The subgroup analysis also displayed no differences between dextrose and corticosteroid (MD = −0.03, 95 % CI: −0.28, 0.23) and non-corticosteroids (MD = −0.17, 95 % CI: −0.44, 0.10), with high heterogeneity for corticosteroid subgroups (I^2 = 74 %, p = 0.03), and low heterogeneity for non-corticosteroids (I^2 = 18 %, p = 0.28).

3.12. Short-time CSA

Eight studies were included for meta-analyses, and two were excluded based on Galbraith, which were the hyaluronic acid arm of Wu [28] and the study by Wu [34]. There were no significant changes in CSA between groups (MD: 0.37, 95 % CI: −0.01, 0.75). Sensitivity analysis revealed that there were notable differences when the Rahimi [30] and NS arm of "Wu" et al. [28] studies were excluded. Heterogeneity was low (I^2 = 0 %, P = 0.84), and the meta-bias was insignificant (P = 0.75).

3.13. Subgroups of short-time CSA

The subgroup analysis included seven studies. Four studies used corticosteroids [29,30,31,33] as a control, and three [28,33,34] used non-corticosteroid treatments (PRP, NS, and hyaluronic acid). The analyses did not reveal significant differences between treatments for both subgroups (MD: 0.35, 95 % CI: −0.05, 0.76, and MD: −0.03, 95 % CI: −0.87, 0.81, respectively), with nonsignificant low and moderate heterogeneity (I^2 = 0 %, P = 0.76, and I^2 = 42 %, P = 0.18, respectively).

3.14. Mid-time CSA

Removing the NS arm of Wu [28] and Wu [34] based on Galbraith plot findings, the meta-analysis for six studies showed no significant differences between groups (MD: 0.43, 95 % CI: −0.01, 0.88) with significant heterogeneity (I^2 = 52 %, P = 0.04). The meta-bias was not significant (p = 0.40), and the sensitivity analysis revealed that removing the PRP and hyaluronic acid arms of "Wu" et al. [28] and the study by "Rahimi" et al. [30] would change the results.

3.15. Subgroups of mid-time CSA

There were no significant differences between the control groups for corticosteroids and non-corticosteroids (MD = −0.21, 95 % CI: −0.67, 0.24, and MD = −0.14, 95 % CI: −2.54, 2.26, respectively), and there was low and high heterogeneity (I^2 = 0 %, P = 0.49, and I^2 = 96 %, P < 0.01).

3.16. Short-time BCTQ-SS

Eight studies had sufficient data for this outcome, including the three arms of Wu [28], still NS arm, and three other studies [31,33,34], which were outliers and dropped. There were no significant differences between groups for the four included studies and the two arms of Wu without heterogeneity (MD: 0.07, 95 % CI: −0.21, 0.35, and I^2 = 0 %, P = 0.72). There was also no publication bias (P = 0.42).

3.17. Subgroups of short-time BCTQ-SS

The subgroup analysis for corticosteroids and non-corticosteroids omitting four studies [31,33–35] of outliers revealed no differences between groups (MD: 0.10, 95 % CI: −0.24, 0.44; and MD: −0.32, 95 % CI: −1.01, 0.37) with low and high heterogeneity (I^2 = 0 %, P = 0.45, and I^2 = 63 %, p = 0.07, respectively).

3.18. Mid-time BCTQ-SS

We removed the four outliers [28,31,33,34] identified by Galbraith's plot. The analysis for two studies by "Aghaei" et al. [29] and "Nasiri" [32] and three arms by "Wu" et al. [28] revealed no differences between groups with moderate heterogeneity (MD = −0.36, 95 % CI: −0.78, 0.05, and I^2 = 43 %, p = 0.14). There was also no meta-bias based on the Egger test (p = 0.27). Omitting "Nasiri" et al. [32] would have changed the results based on sensitivity analysis.

3.19. Subgroup of mid-time BCQT-SS

Omitting four outliers [24,27,33,34], the subgroup analysis for corticosteroids and non-corticosteroids revealed no difference between groups (MD: −0.04, 95 % CI: −0.72, 0.64, and MD: 0.47, 95 % CI: −1.16, 0.24, respectively) with low and high heterogeneity (I^2 = 17 %, P = 0.27, and I^2 = 63 %, P = 0.07).

3.20. Short-time BCTQ-FF

Seven studies, including "Wu" et al.'s [24], three arms, were analyzed. Two studies were outliers [26,34] and were removed. The meta-analysis revealed a significant difference in favor of dextrose (MD: −0.48, 95 % CI: −0.83, −0.14) with moderate nonsignificant heterogeneity (I^2 = 30 %, P = 0.06). There was no meta-bias (P = 0.73).

3.21. Subgroup of short-time BCTQ-FF

Removing four outliers [24,26,33,34] including the PRP arm of Wu et al. [24], the analysis revealed non-significant difference with low heterogeneity versus corticosteroids and significant differences in favor of the dextrose group with high heterogeneity (MD: −0.08, 95 % CI: −0.51, 0.36 with I^2 = 0 %, P = 0.64, and MD: −1.12, 95 % CI: −1.78, −0.46, with I^2 = 72 %, P = 0.01, respectively).

3.22. Mid-time BCTQ-FF

Excluding four outlier studies [24,26,33,34], the results showed a significant difference between groups in favor of dextrose efficacy (MD: −0.46, 95 % CI: −0.76, −0.16), with low heterogeneity (I^2 = 17 %, P = 0.31). The meta-bias was insignificant (P = 0.45). In subgroup analysis, four studies were outliers [25, 27, 29, 31] and removed. There was a trend toward dextrose versus corticosteroids that was non-significant (MD: −0.43, 95 % CI: −0.87, 0.00) without heterogeneity (I^2 = 0 %, P = 0.70), and a significant difference in favor of dextrose versus non-corticosteroids with high and significant heterogeneity (MD: −0.65, 95 % CI: −1.03, −0.26, and I^2 = 82 %, P < 0.01).

4. Discussion

The findings of our review and meta-analysis demonstrated that DEW may be superior to other injections in pain relief and functional outcomes, especially in the mid-term (more than four weeks). Based on the outcomes, we will discuss our findings in detail.

4.1. Pain

In short-term findings, only compared with non-corticosteroids, DEW significantly reduced pain. Comparing DEW to corticosteroids, the two injections had no superiority in pain reduction. In mid-time findings, DEW was superior to all controls, as well as in subgroup analysis versus corticosteroids. The time-to-effect of each injectate on peripheral nerve entrapment is not yet evident. Based on the available evidence, we can speculate that corticosteroids' main mechanism of action for peripheral nerve compression lasts one to three months [36]. In contrast, DEW studies have shown long-term effects on pain and function improvements, as well as possible two-week analgesic effects due to the post-injection inflammatory response [31,37]. These findings align with our mid-term results, which show DEW to be superior to all controls.

4.2. Nerve conduction studies

No significant difference was evident in the DSCV and DML meta-analyses. In most of the included studies, both injections were effective in improving these findings. The results of nerve conduction studies may take much longer than other outcomes to return to normal values. The sensitivity and specificity of nerve conduction findings are highly reliable for the diagnosis of CTS [38–40]. However, we must be more careful in interpreting the outcomes regarding post-treatment or follow-up assessments. An expert opinion by "Soreide" et al. [41] suggests the use of neurophysiological testing (EDX) before injection and surgical treatments. They believed that using this diagnostic value may better help track any improvements after treatments rather than tracking the improvements. This may be related to the normal EDX findings in some diagnosed CTS patients, the prolonged (12 months or more) period of normalization of EDX findings, and finally, after neuroregeneration, some may not duplicate the premorbid state and thus may never return to normal values. A study by "Ho" et al. also found the DSCV findings at baseline to be a prognostic factor for the good or poor outcomes of DEW injection based on post-injection VAS findings [37].

4.3. Nerves in ultrasonography

Short-term changes between the groups were not prominent. At this time point [<4 weeks], we may not expect a remarkable decrease in neural edema; however, from sensitivity analysis, we can find a significant difference in favor of control (including corticosteroid, NT, and PRP), when omitting the study by "Soltani" et al. [34]. Differences in the medium term were also non-significant, with sensitivity analysis revealing a difference when omitting the PRP and hyaluronic acid arms of "Wu" et al. [24] and

"Bahrami" et al. [24]. The study by "Wu" et al. [26] is the only study with preliminary severe cases of CTS. Removing this study along with "Bahrami" et al. [24] would change the results in favor of dexmed in mid-term findings (3–24 weeks). However, there are some remarkable factors to be considered when interpreting the findings of CSA. "Bell" et al. [42] found influential factors in the diagnostic accuracy of ultrasonography. One could depend on the expertise of the sonographer and possible human error. Another important factor is the anatomical region of sonography, which was best described for CTS as the inlet of the carpal tunnel (CT) at the distal edge of the radial-ulnar joint, and based on our results, all CTS studies were consistent with this standard. Still, "Bell" et al. believed that measurement of the largest CSA across the entire CT might be more accurate as the swollen part may not necessarily be present at the pisiform level and vary across patients. They also claimed that reporting the average of repeated CSA measurements might have more accuracy than only one. Repeated measurement was reported in studies included in the CSA meta-analysis [14,26,31,38], except for "Yoshii" et al. [31] and "Bahrami" et al. [24].

4.4. Function

The available eligible studies with sufficient information on the findings of the Boston questionnaire were scarce. For the symptom severity scale, there was no difference between the groups in terms of symptom relief based on the questionnaire findings. However, for functional improvements, dexmed was superior at all time points for all control groups. In the subgroup analysis based on corticosteroids and non-corticosteroids, dexmed was superior only to non-corticosteroids. There was also a nearly significant difference in favor of dexmed in medium term versus corticosteroids, which is still not meaningful. There are two different pain scales for outcomes. One is VAS, and the other is BCTQ symptom severity. We observed improvements in pain in favor of dexmed; however, there were no differences in the latter. This difference is incomparable with different scales. The VAS scores the pain with a measure of ten points, but the BCTQ-SS not only measures pain but also numbness, weakness, tingling, and difficulty grasping. That's why comparing these outcomes or considering the latter as a pain measurement tool is not possible.

4.5. Long-term findings

Two long-term follow-up retrospective studies on the effectiveness of dexmed for CTS, without control groups, reported remarkable outcomes. The first one was in 2011 by "Li" et al. [13], who studied 135 patients and found 88.6 % effective outcomes after ½–3 years post-injection. They also had 15 patients with previous failed surgical interventions, and at follow-up, they found that 80 % of them had effective outcomes. The second study in 2022 by "Chen" et al. [28] included 36 previously treated patients, 15 of whom were similar to the first study [13]. They followed the patients after a mean of 33 months post-injection and found that 93.1 % of them had effective outcomes. No patient required further surgical treatment. Eleven patients required additional conservative management, such as rehabilitation, medication, and acupuncture. These two studies are the only available literature on the long-term findings of dexmed injection.

4.6. Recent evidence and recommendations

A recent network meta-analysis in 2023 [43] found PRP to be the most effective compared to DEW and corticosteroids, evaluating the VAS and Boston questionnaire outcomes among CTS patients. This is different than our findings. However, it is notable that in their 12 included studies, only four used DEW, while in our study, we extracted data from 12 studies using DEW, which makes our evidence stronger, more recent, and reliable with larger studied sample sizes. These results also pertain to the short-term (3 months) findings, in which we previously discussed that dexmed may worsen pain at the beginning of treatment and may not be the ideal tool to compare efficacy. Comparing surgical interventions to less invasive choices (such as endoscopic interventions and various injections), the latter is found to be more effective with fewer side effects and quicker return to daily activity [3,44]. However, the most recent systematic review in 2024 [44] could not identify the differences between each injectate's efficacy due to a lack of meta-analysis, which is covered in our study.

Our findings from up to six months of follow-up indicate that ultrasound-guided dexmed injection is not only safe but also more effective than other injectants, such as PRP (platelet-rich plasma), corticosteroids, and normal saline, for treating carpal tunnel syndrome (CTS) and show severe entrapment with the fewest side effects. This evidence can assist clinicians in making initial treatment choices that are less invasive and more efficient.

4.7. Limitations

Various factors, including the use of ultrasound guidance, the degree of nerve entrapment, co-interventions such as night splints, and rehabilitation, can significantly influence the outcomes of injections. One of our limitations was the variety of these factors. Fortunately, only one RCT [34] used landmark-based injections; the rest were administered under ultrasound guidance. The lack of long-term findings in studies is a significant limitation, as it could help identify variations between frequently administered injectates and their efficacy. Variations in dosages can significantly impact results. A standard protocol based on clinical and pharmaceutical studies for precise and safe injectate doses is needed to achieve better results with fewer side effects. Another limitation is the scarcity of randomized control trials. Retrospective studies are available on this topic; however, we could not use their outcomes for meta-analysis. This topic requires additional long-term follow-up prospective randomized control trials, comparing the outcomes of DEW with those of other injectates under ultrasound guidance and more precise reporting of adverse effects.

Despite these limitations, our study is unique in that it examines the literature on nerve entrapments in the upper limbs (as opposed to prior systematic reviews that exclusively examined CTS) and assesses all relevant outcomes, including nerve conduction findings and CSA, which have not been thoroughly examined in prior systematic reviews.

5. Conclusion

According to this meta-analysis, dextrose injection is an effective therapeutic option for managing pain and restoring function in cases of entrapment neuropathies. However, further high-quality studies are needed to confirm these findings and establish optimal dosing regimens and injection protocols. Healthcare providers should consider incorporating dextrose injections into their treatment armamentarium for patients with entrapment neuropathies.

CRediT authorship contribution statement

Fatemeh Azizi: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Data curation, Conceptualization. **Fatemeh Saber Ghamsari:** Writing – review & editing, Writing – original draft, Visualization, Resources, Project administration, Methodology, Investigation, Data curation. **Fereshteh Eidy:** Writing – original draft, Methodology, Formal analysis. **Sama Heidari:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation, Data curation. **Nastaran Maghbouli:** Writing – review & editing, Writing – original draft, Validation, Supervision, Project administration, Conceptualization. **Shirin Djalalinia:** Conceptualization. **Amir Kasaeian:** Formal analysis.

Ethical statement

Our systematic review did not conduct any trials involving humans or animals; therefore, we did not require any ethical approvals.

Data availability

Extracted data will be available upon reasonable request from the corresponding author, Nastaran Maghbouli. Please contact the email address nmaghbouli@sina.tums.ac.ir.

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Declaration of competing interest

We declare that there are no conflicts of interest associated with this publication. We have no financial, personal, or professional interests that could be construed to have influenced the work reported in this article. All research was conducted independently, and no external parties had any influence on the design, execution, or reporting of the study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2025.e41822.

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