INFORMATION BRIEF (RAPID REVIEW)

PERINEURAL 5% DEXTROSE INJECTION THERAPY FOR NEUROPATHIC PAIN

Malaysian Health Technology Assessment Section (MaHTAS)
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TITLE: PERINEURAL 5% DEXTROSE INJECTION THERAPY FOR NEUROPATHIC PAIN

PURPOSE

To provide brief information on the effectiveness, safety and cost-effectiveness of perineural 5.0% dextrose injection therapy for treatment of neuropathic pain based on request from the Medical Practice Division, Ministry of Health Malaysia.

BACKGROUND

The International Association for the Study of Pain describes neuropathic pain as pain that arises due to direct consequence of a lesion or diseases affecting the somatosensory system. In contrast to tissue damage, such as muscle or ligament injuries frequently incurred by twisting the back, neuropathic pain arises from direct damage to the nerve itself. This pain can lead to hypersensitivity, causing even little stimuli to be uncomfortable. Even simple tasks like eating, drinking and brushing teeth can cause severe agony, making it hard to live a regular life.[1] The prevalence rates of neuropathic pain as a worldwide clinical entity ranged between 0.9% and 17.9%,[2] increasing to roughly 20.0% to 30.0% in patients with diabetes.[3-6] Meanwhile in Malaysia, the frequency of neuropathic pain varies between ethnic groups. Of the 210 patients, 26 (12.4%) had neuropathic low back pain and it is connected with non-Chinese ethnicity and a higher body mass index.[7]

Current management of neuropathic pain includes drugs which consist of anti-epileptics, tricyclic antidepressants, selective serotonin reuptake inhibitors and norepinephrine reuptake inhibitors. These medications have somewhat higher adverse effects compared to typical painkillers like paracetamol and non-steroidal anti-inflammatory drugs.[8,9] Furthermore, corticosteroid injections are routinely used to control pain, with demonstrated short-term effects and mixed outcomes. Unfortunately, corticosteroid injections can cause complications such as neural toxicity, skin thinning, tendon rupture and tissue atrophy.[10,11] Long-term use should be accompanied by monitoring for potential adverse effects of these treatments. Nerve blocks and narcotic medications may be used as a second line of therapy if first pharmacological therapies fail.[1]

In terms of local practise, the Malaysian Association for the Study of Pain had successfully published Malaysian Guidelines on Management of Neuropathic Pain (Second Edition) in 2012. Pharmacotherapy (such as anticonvulsants, antidepressants, opioids and local anaesthetics) is the most common first-line treatment option for neuropathic pain. The other treatment strategies such as physical and occupational therapy, psychological therapy, interventional therapy (e.g. surgical procedures, sympathetic block, epidural steroid injection, intrathecal therapy and spinal cord stimulation) and complementary therapies (e.g. massage, hypnosis, acupuncture and herbal medicine) should be in conjunction with drug therapy in a multi-disciplinary treatment program. In rare circumstances, a non-pharmacological therapy strategy may be considered as a first-line treatment option.[12]

Over recent years, perineural injection therapy (also known as Lyftogt technique/ neural prolotherapy) as shown in **Figure 1** has been introduced as one of the most recent achievements in regenerative medicine. It targets neurogenic inflammation in the subcutaneous nerves, which can cause discomfort. The treatment was further enhanced by administering 5.0% dextrose injections, which offered significant pain relief in 300 cases with Achilles tendinopathy.[13] The process is hypothesised to limit transient receptor potential

vanilloid 1 (TRPV1) expression, resulting in the release of substance P and calcitonin gene related peptide (CGRP), to reduce neurogenic inflammation **(see Figure 2)**.[14]

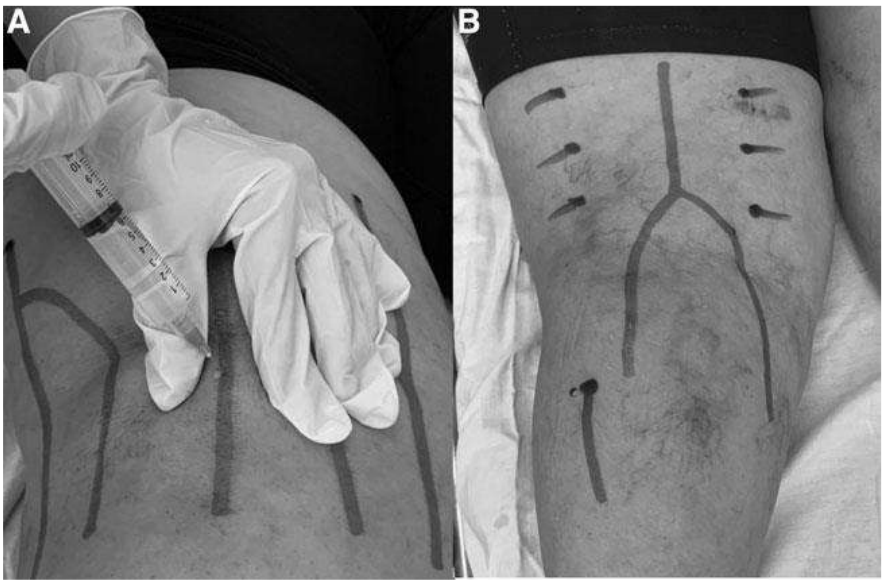


Figure 1: Points of chronic constriction (where the cutaneous nerve passes through) were identified by locating pain locations along the sensory nerves' path to the respective site. The site was prepared using aseptic and antiseptic techniques after the painful spots were identified and marked. At these locations along the nerve route, 5.0% dextrose solution was administered subcutaneously adjacent to the nerves.[15]

Hydrodissection with 5.0% glucose water for peripheral entrapment neuropathy can be divided into mechanical and pharmacological effects. Detaching the nerve through a non-specific effect of fluid under force may gradually lessen adhesions, increase blood flow and remobilise the nerve for neuroregeneration. However, understanding the better effects of glucose as an injectate for hydrodissection requires a deeper knowledge of its pharmacological mechanism.[16-20] Several studies have postulated that glucose increase through a possible sensorineural mechanism, stabilises neuronal activity or reduces neurogenic inflammation, therefore alleviating neuropathic pain. When the nerve is in a hypoglycaemia environment, histopathological changes occur in peripheral nerves, accompanied with the activation of nociceptive C-fibers and enhanced noxious signal transduction.[21,22]

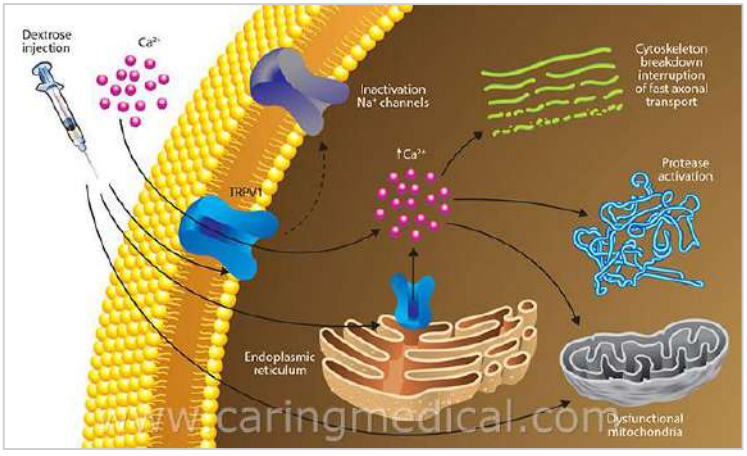


Figure 2: Perineural injection into sensitised peptidergic nerve – the injections are believed to restore the normal function of the TRPV1 receptor on sensory neurones in the pain pathway. These nerves then assist to repair the tissue they innervate.[23]

Furthermore, perineural injection therapy is an outpatient technique that takes only a few minutes to finish and does not require any incisions. The recovery time is relatively short, with most patients able to resume regular activities the next day (but the underlying disorders causing nerve pain may preclude this). The therapy may be recommended to address pain signals resulting from the following disorders:[24]

- Carpal tunnel syndrome and certain other occupational injuries
- Plantar fasciitis
- Various types of sports injuries, such as Achilles tendinopathy
- Various types of overuse injuries, such as tennis elbow
- Certain surgical injuries
- Certain traumatic injuries
- Fascial adhesions
- Osteopathic arthritis
- Chronic migraine
- Certain other painful conditions of the muscles, tendons and ligaments

Although perineural injection therapy has wide variety of potential applications, not all patients are suitable candidates. Any final treatment decisions should always be carefully discussed with a board-certified, licensed healthcare professional.[24]

EVIDENCE SUMMARY

The systematic review was conducted. A total of 283 titles were retrieved through the Ovid interface: Ovid MEDLINE® All <1946 to 27 November 2024>, PubMed and United States of Food and Administration. Google was used to search for additional web-based materials and information. There was no language limitation in the search and the last search was conducted on 29th November 2024. There were eight randomised controlled trials and three retrospective studies were found to be relevant and included in this review. The studies were conducted in South Korea, Taiwan, China, Mexico, Hawaii, Egypt and Turkey.

EFFECTIVENESS

Three studies enrolled patients with carpal tunnel syndrome, four studies on lower limbs and four studies on other neuropathic pain sites. The findings are summarised in **Table 3**.

a. Carpal tunnel syndrome

Lin MT et al. (2021) conducted a randomised controlled trial to investigate the effect of different injection volumes on ultrasonographic parameters and correlation to clinical outcomes under perineural 5.0% dextrose injection from June 2018 to December 2019. Forty-five patients (aged 20 to 80 years old) from National Taiwan University Hospital were randomly assigned to receive either 1 mL (n=14), 2 mL (n=14) and 4 mL (n=17) of 5.0% dextrose water, corresponding to ultrasound-guided perineural injection therapy. Patients who had been diagnosed with idiopathic carpal tunnel syndrome and fulfilled the electrophysiological criteria and clinical trial were included. They might take paracetamol after the injection, but they were not permitted to take neuropathic painkillers or non-steroidal anti-inflammatory medication. Any extra night splints, occupational therapy or physical therapy were not provided.[25, level I]

In terms of ultrasonography outcomes within groups, cross-sectional area (CSA) of median nerve in the 2 mL group (p=0.005) and the 4 mL group (p=0.015) substantially declined from

baseline data at all follow-up time-points (1-, 4-, 12- and 24-week). After the post-hoc analysis, the 4 mL group showed significant improvements in mobility at 1-, 4- and 12-week ($p<0.05$), and also in elastography at 24-week ($p=0.042$) as compared to baseline. Additionally, clinical outcomes showed a substantial improvement in visual analogue scale (VAS) and Boston Carpal Tunnel Syndrome Questionnaire (BCTQ; the score consists of eight questions on the functional status scale and 11 questions on the symptom severity scale. On a scale of one to five, higher numbers indicated more severe conditions and the inability to carry out certain tasks) across all time points in all three groups. By comparing between groups at the first week after injection, the 4 mL group's mean change improved more than the other groups in VAS ($p=0.023$), BCTQ ($p=0.002$) and mobility (4 mL: 0.35 [0.58], 2 mL: -0.12 [0.56], and 1 mL: 0.01 [0.39], $p=0.04$), and represented significant clinical improvement at fourth weeks after injection from baseline. According to the results, perineural injection treatment with a larger volume of 5.0% dextrose may temporarily increase median nerve mobility.[25, level I]

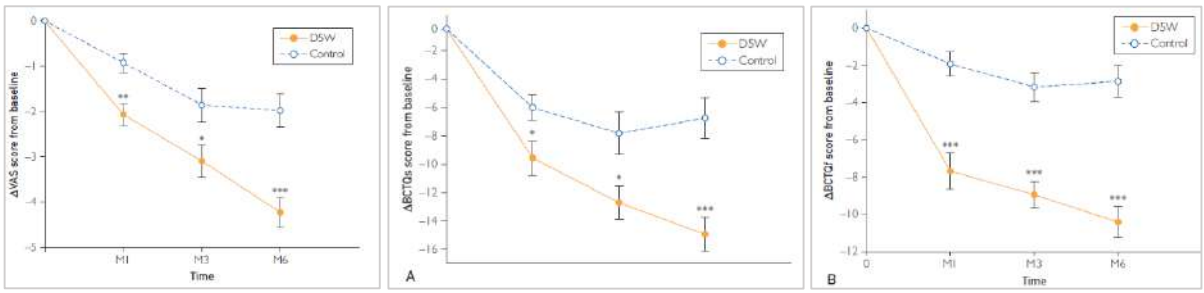
Another **randomised controlled trial was conducted in China, by Shen YP et al. (2019)** to compare the 6-month outcome of perineural injection with 3 mL platelet rich-plasma (n=26) or 5.0% dextrose (n=26) in patients with moderate carpal tunnel syndrome from February 2016 to July 2017. The study included patients aged 20 to 80 years old with unilateral moderate carpal tunnel syndrome, with the presence of these symptoms for a minimum of three months; a) paresthesia/ dysesthesia with awkward weakness of the hand aggravated by rhythmic activity of the wrist or during sleep, with symptom relief after hand shaking or postural modification, b) impaired sensation in the territory of the hand innervated by the median nerve, c) reduced strength with wasting of the thenar muscles and d) positive Phalen's test ± Tinel's sign. Both groups received 3-cc perineural injection under ultrasound-guidance that was conducted by a 5-year experienced physician in the respective treatment.[26, level I]

The findings reported that, there were significant improvements in both groups in symptom severity scale, functional status scale and CSA, at each follow-up time-point (1-, 3- and 6-month) when compared to baseline ($p<0.05$). The functional status scale at three months ($p=0.044$), distal motor latency at six months ($p=0.028$) and CSA of the median nerve at three and six months post-injection ($p=0.010$ and 0.018, respectively) all showed significantly greater improvements in the platelet-rich plasma group compared to the dextrose group.[26, level I]

Wu YT et al. (2017) in another randomised controlled trial assessed the 6-month effectiveness of ultrasound-guided perineural injection therapy using 5.0% dextrose in patients with mild-to-moderate carpal tunnel syndrome, in a single medical centre in Taiwan. Forty-nine patients (aged 58.47±2.33 in dextrose group, 58.10±1.93 in control group) who were diagnosed with mild-to-moderate carpal tunnel syndrome on the basis of an electrophysiological analysis, and who had onset symptoms that had persisted for at least six months, were randomly assigned. Both groups had one session of ultrasound-guided perineural injection therapy; the dextrose patient group (n; treated wrist=30) received 5-cc of 5.0% dextrose water, and the other 30 treated wrists received 5-cc of normal saline.[27, level I]

Compared with the scores of the control group, the study showed significant improvements in:[27, level I]

- The VAS **(see Figure 3a)** at 1-month ($p=0.001$), 3-month ($p=0.02$) and 6-month ($p<0.001$).
- The BCTQ severity scores **(see Figure 3b)** at 1-month ($p=0.02$), 3-month ($p=0.01$) and 6-month ($p<0.001$).
- The BCTQ function scores **(see Figure 3c)** at 1-month, 3-month and 6-month ($p<0.001$).



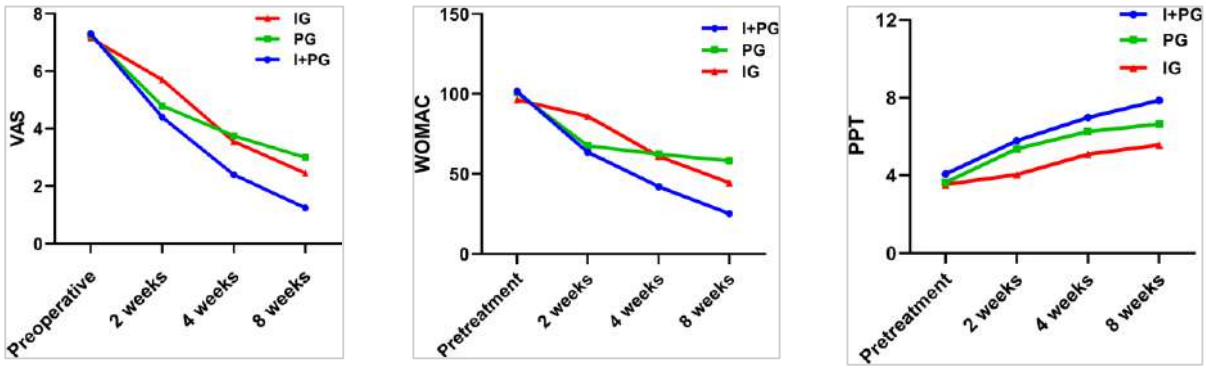
(a) **(b)** **(c)**

Figure 3: a) Mean change at baseline and post-injection in VAS results in both groups (mean ± standard error), b) mean difference at baseline and post-injection in BCTQ severity scores and c) BCTQ functionality scores in both groups (mean ± standard error).[27, level I]
**p<0.05; **p<0.01; ***p<.001; an independent t-test was used. D5W=5% dextrose; M=month; VAS=visual analog scale, BCTQ=Boston Carpal Tunnel Syndrome Questionnaire*

b. Lower limbs

In a **randomised controlled trial that was conducted by Fu Y et al. (2024)** in China**,** the study aimed to compare the efficacy of intra-articular prolotherapy combined with peri-articular perineural injection in the management of knee osteoarthritis. This double-blind clinical trial involved 60 patients with these inclusion criterias: aged 48 to 80 years old, knee osteoarthirtis diagnosis, Kellgern–Lawrence grading scale grades two and three, and knee joint stiffness, discomfort and crepitation that has persisted for at least three months. Under ultrasound supervision, all patients were split into three groups and given either intra-articular prolotherapy (n=20; 8 mL of 20.0% dextrose), peri-articular perineural injection (n=20; 2 mL of 5.0% dextrose) or combination of both treatments (n=20).[28, level I]

Following two weeks of therapy, the VAS and Western Ontario McMaster University Osteoarthritis Index (WOMAC; to evaluate knee function) scores of the peri-articular perineural injection and combination therapies groups were significantly lower than intra-articular prolotherapy group (p<0.05). However, eight weeks after therapy showed only the combination therapies group demonstrated significantly lower VAS and WOMAC, and higher pressure pain threshold as compared to other two therapies (p<0.05), see **Figure 4**. Additionally, the study revealed that the combined therapies improved knee joint function and discomfort more than one therapy alone. As compared to intra-articular prolotherapy, peri-articular perineural injection would have a faster analgesic impact and superior early effectiveness. This might have related to the different mechanisms between two therapies. [28, level I]



(a) **(b)** **(c)**

Figure 4: The results of the three groups at 2-, 4- and 8-week after therapies. a) The VAS scores, b) the WOMAC scores and c) the pressure pain threshold scores.[28, level I]

Another **randomised controlled trial that involved lower limbs was carried out by Garcia-Triana SA et al. (2020)** in Mexico from January 2017 to May 2018. The study evaluated the efficacy of perineural injection therapy of 0.5 to 1 mL 5.0% dextrose, combined with home physical therapy program (n=25; 49 knees) in patients with a diagnosis of chondromalacia patella compared with a control group receiving physical therapy only (n=25; 50 knees). Men and women (aged 25 to 70) who had been clinically and radiographically diagnosed with grade II or III chondromalacia patella, with or without gonarthrosis, met the inclusion criteria.[15, level I]

The outcomes of the between-group analysis are demonstrated in **Table 1**. As shown in the red boxes, some variables in both groups had substantial changes after the therapies. **Figure 5** shows the mean between-group difference comparison following treatment.[15, level I]

Table 1: Between-group comparison of WOMAC, VAS, and flexion and extension movements before and after treatment with physical therapy with or without perineural injection treatment.[15, level I]

	PIT + PT group (n=25)			*PT group (n=25)*			*p-Value after treatment in study and control groups*
	Before treatment	*After treatment*	*Change score*	*Before treatment*	*After treatment*	*Change score*	
WOMAC pain	11.2±2.9	3.8±2.2	7.3±3.5	9.6±3.3	6.3±2.9	3.2±2.9	<0.010
WOMAC stiffness	4.2±1.8	1.1±1.5	3±1.69	4.3±1.3	2.7±1.8	1.6±1.5	<0.010
WOMAC functional capacity	36.9±9.9	13.7±8.3	23.2±10.7	32.5±8.3	21.3±9.5	11.1±8.9	<0.010
WOMAC total	51±13.8	17.8±10.8	33.1±15.6	46.3±11.9	29.6±12.1	16.7±12.7	<0.001
VAS pain score	7.5±1.6	2.3±1.4	5.2±2	7.0±1.4	4.5±1.6	2.5±1.98	<0.001
Right side flexion	113.40±9.9	115.5±9.2	2.12±3.51	111.6±11.1	113.5±9.6	1.92±3.17	0.457
Left side flexion	113.3±8.4	116.5±9.3	3.20±4.66	112.2±11.4	114.8±9.3	2.52±3.53	0.520
Right side extension	−0.60±1.6	−0.12±0.6	0.48±1.41	−1.16±2.96	−0.40±2	.76±2.33	0.506
Left side extension	0.60±1.6	−0.12±0.6	0.48±1.41	0.68±1.6	0±0	−0.68±1.62	0.322

Flexion and extension angles were measured in degrees.
PIT, perineural injection treatment; VAS, visual analog scale; WOMAC Index, Western Ontario and McMaster Osteoarthritis Index

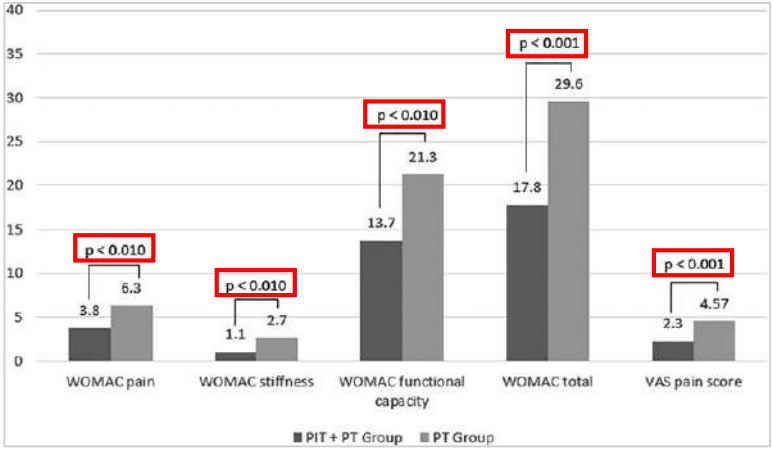


Figure 5: The WOMAC Index and VAS score comparisons between groups.[15, level I]

Alyan II et al. (2018) in another randomised controlled trial was conducted in Egypt, compared the benefit of perineural injection therapy with 5.0% dextrose and low level laser therapy on pain modulation in patients suffering from chronic knee osteoarthritis. One hundred patients (aged 40 to 70 years) who dissatisfied with previous attempts at conservative treatment including non-steroidal anti-inflammatory drugs were randomly assigned (1:1) from November 2016 to December 2017. The treatment group received 0.5 mL of 5.0% dextrose in sterile water, meanwhile treatment provided for another group included low level laser therapy on eight points, with a dose of an energy of 6 Joule per point for 60 seconds, with a

total dose of 48 Joule in each session. At the end of therapy, the VAS and WOMAC scores significantly improved ($p<0.001$, $p<0.0001$) representing in the perineural injection therapy group, compared to group receiving low level laser therapy.[29, level I]

A **retrospective study was conducted by Guzel I et al. (2021)** in Turkey, to evaluate the effectiveness of perineural injection therapy in the management of chronic post-surgical pain after total knee arthroplasty. Sixty patients (aged 40 to 90 years old) who underwent total knee arthroplasty for knee osteoarthritis between January 2017 and July 2018 were included in this study. Thirty-one patients received three rounds of perineural injection therapy (3 mL of 5.0% dextrose) in addition to standard post-operative total knee arthroplasty protocol, which included oral and intravenous analgesics, and rehabilitation programs (experimental group). In contrast, a similar age- and gender-matched group of 29 patients received standard post-operative protocol, which included oral and intravenous analgesics, and rehabilitation programs (control group). Following 21 days of surgeries, anti-inflammatory drugs were prohibited except for acetaminophen, which could be used a maximum four times a day at 500 mg when the pain became unbearable.[30]

Significant improvements ($p<0.001$) were observed in both groups regarding on WOMAC and VAS scores across all repeated measurements. In every follow-up period (1-, 3- and 6-month), the scores in the experimental group were significantly higher than the control group ($p<0.001$). The study revealed that the perineural injection therapy group improved pain and functional scores better than those in the control treatment group.[30]

c. Other neuropathic pain sites

Chen LC et al. (2020) conducted a randomised controlled trial to assess the effects of perineural corticosteroid and 5.0% dextrose water injections in patients with ulnar neuropathy at the elbow, from March 2017 to October 2019 in Taiwan. Thirty-six patients (aged 20 to 80 years) with diagnosis of mild to moderate ulnar neuropathy, clinically confirmed through electrophysiological study were randomly assigned to dextrose group (n=18; 5 mL of 5.0% dextrose) and steroid group (n=18; 3 mL of triamcinolone acetonide 10 mg/mL, plus with 2 mL of normal saline). From two weeks before to participation until the end of the follow-up period, all additional conservative treatments such as physical therapy, analgesic medicine, local injection and acupuncture, were prohibited. Acetaminophen (500 mg, up to four days) was the only medication used as a rescue medicine when required.[31, level I]

Most measures including VAS and CSA showed significant improvements in both groups at each follow-up time-point (1-, 3-, 4- and 6-month) compared to baseline ($p<0.05$). However, the difference between groups showed no significant result even though the dextrose group demonstrated larger reductions in symptoms severity and CSA from the third month to the end of follow-up.[31, level I]

The short-term analgesic effects of 5.0% dextrose injection and saline for non-surgical chronic low back pain were assessed by **Maniquis-Smigel G et al. (2017) in a randomised controlled trial** from February to November 2013**.** Inclusion criteria included the 19 to 75 years old patients living in Hawaii, contemporaneous involvement in a patient trial of a vertical tiny needle caudal epidural injection method, and six months or more of self-reported moderate-to-severe chronic low back pain, including below the iliac crest as determined by self-reported scores. Nineteen patients received 10 mL of 5.0% dextrose and sixteen received 10 mL of normal saline injections into the caudal epidural region. The patients were treated in a prone posture without an abdominal bolster or reverse Trendelenburg. The injection site was sterilised with 2.3% chlorhexidine gluconate and 24.0% isopropyl alcohol. A 25 gauge 3.8 cm needle was used with an entrance point at or below the sacral cornua to inject in the caudal epidural space. Patients received no post-injection analgesics and could continue taking their current medications during the 2-week study period.[32, level I]

The dextrose group outperformed the saline periods, with the exception of two weeks as shown in **Figure 6**. There were significant differences in scores after 15 minutes (4.4±107 vs. 2.4±2.8; p=0.015), two hours (4.6±1.9 vs. 1.8±2.8; p=0.001), four hours (4.6±2.0 vs. 1.4±2.3; p<0.001) and 48 hours (3.0±2.3 vs. 1.0±2.1; p=0.012). The dextrose group had a greater rate of experiencing more than 50.0% reduction in pain after four hours (16/19; 84.0%) compared to saline group (3/16; 19.0%; p<0.001).[32, level I]

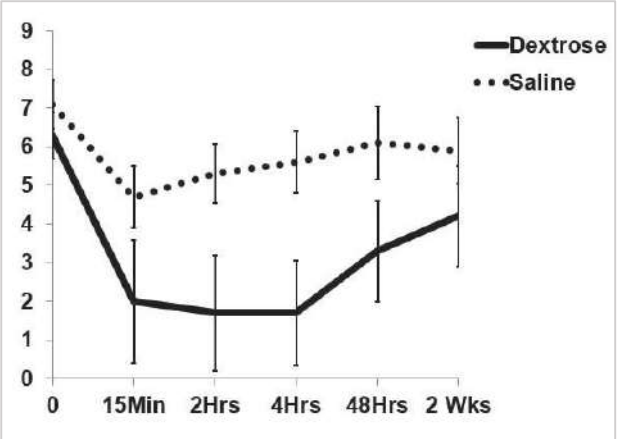


Figure 6: Change in zero to 10 numerical rating scale pain scores over two weeks (±standard error). The rating scale pain is scored on a range of zero to 10 points, with 10 anchored by "worst pain imaginable" and zero by "no pain". Non-overlapping confidence intervals indicate significance of change in dextrose scores compared with change in score of the saline (p<0.05) group.[32, level I]

In a **retrospective study** that was conducted in Pusan National University Hospital, South Korea, **Kim H et al. (2024)** compared the effects of perineural injection therapy with dextrose or lidocaine on neuropathic pain. Data were taken from a pain clinic database from August 2019 to December 2022, with aged 40 to 72 years old. No personal information was included. The study included patients with postherpetic neuralgia (PHN, n=26), trigeminal neuralgia (TN, n=18), complex regional pain syndrome (CRPS, n=28) or peripheral neuropathy (PN, n=40) who had undergone perineural injection therapy with buffered 0.5 to 3 mL of 5.0% dextrose (dextrose group, n=89) or 0.5% lidocaine (lidocaine group, n=23) for pain control. Due to the small number of patients in the lidocaine group, statistical analysis was not possible. Hence the trend was only noticed for each disease. Data on pain score, side effects and satisfaction rating (excellent, good, fair or bad) were obtained one week after each therapy and two weeks after the last therapy.[1]

The results reported that, the numerical rating scale pain score decreased significantly in dextrose group only as compared to baseline, in patients with PHN (-27.4±8.6% to -38.6±8.2%; p<0.01), TN (5.9±0.6 to 3.7±0.7; p<0.05) and PN (5.7±0.4 to 3.8±0.3; p<0.01). Additionally, **Figure 7** illustrated the satisfaction improvement in both intervention groups of patients with PHN, TN, CRPS and PN. The study revealed that perineural injection therapy with dextrose decreased pain in PHN, TN and PN, but not in CRPS.[1]

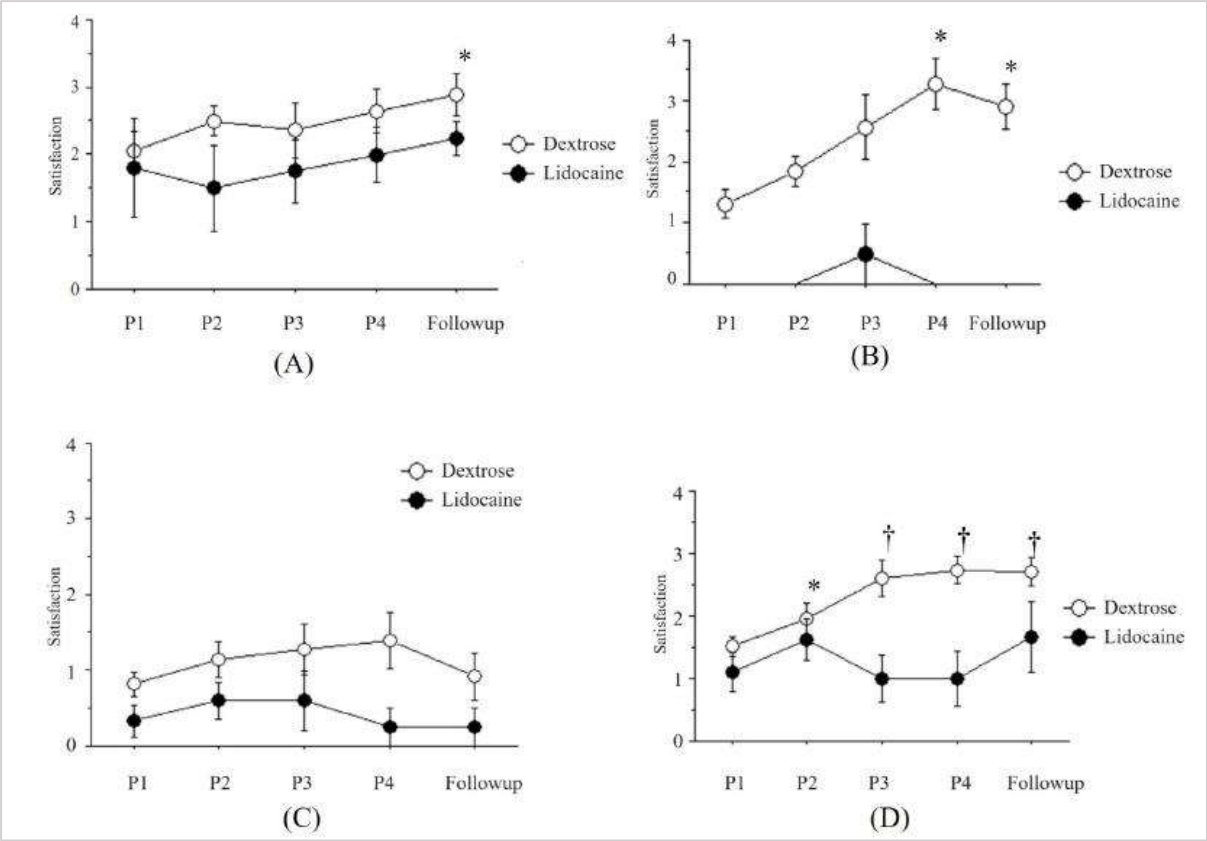


Figure 7: The changes of satisfaction after perineural injection therapy with buffered 5.0% dextrose or 0.5% lidocaine. (A) Post-herpetic neuralgia, (B) trigeminal neuralgia, (C) complex regional pain syndrome, (D) peripheral neuropathy.[1]
*P1: one week after the first therapy. P2: one week after the second therapy, P3: one week after the third therapy, P4: one week after the fourth therapy. Follow-up: two weeks after the fourth therapy. *p<0.05, †p<0.01 vs. the satisfaction after the first therapy in dextrose group.*

Uslu EY (2024) in a retrospective study conducted ultrasound-guided steroid injections on 16 patients and dextrose injections on 17 patients with the diagnosis of superior cluneal nerve (cause of low back pain) neuropathy at Elazig Fethi Sekin City Hospital Polyclinics, Turkey, between September 2023 and March 2024. The study comprised patients aged 18 to 60 who had a positive diagnostic injection test and experienced pain that did not respond to oral medications. The steroid injection group received 2.63 mg betamethasone sodium phosphate plus 5 mg betamethasone dipropionate, whereas the dextrose group received 5-cc of 5.0% dextrose injection. Patients were advised to perform superior cluneal nerve shift, posture and pelvic tilt exercises following the injection. The study found that, dextrose injection outperformed steroid injections in VAS and Rolland-Morris Disability Questionnaire (RMDQ; to assess self-rated physical disability caused by low back pain. For a total score ranging from zero to 24; higher scores represent higher levels of pain-related disability) at one week after therapies **(see Table 2).**[33]

Table 2: Comparison of VAS and RMDQ scores before and one week after the procedure in the dextrose and steroid groups.[33]

Parameter	Dextrose Group (n=17)	Steroid Group (n=16)	p
Preprocedure VAS (mean±SD)	5.81±0.98	6.13±0.957	0.278
1st week VAS (mean±SD)	1.63±1.08	2.50±0.516	0.016
Preprocedure RMDQ (mean±SD)	13.31±1.92	13,38±1.147	0.378
1st week RMDQ (mean±SD)	4.31±1.62	5,81±1.328	0.009

Table 3: The effectiveness of perineural 5.0% dextrose injection therapy for neuropathic pain.

Study	Patient characteristic	Follow up duration	Intervention		Findings
			Treatment	Control	
Carpal tunnel syndrome					
Lin MT et al. 2021 RCT Taiwan[25]	N=45 20 to 80 years	1, 4, 12 and 24 weeks	N=17 4mL 5.0% dextrose	N=14 (1 mL) and n=14 (2 mL) 5.0% dextrose	From baseline • 4 mL group showed significant improvements in mobility at 1-, 4- and 12-week (p<0.05), and in elastography at 24-week (p=0.042). Within group • CSA of median nerve in the 2 mL group (p=0.005) and the 4 mL group (p=0.015) substantially declined at all follow-up time-points. Between-groups (as compared to control) • At 1-week after injection, the 4 mL group's mean change improved more than the other groups in VAS (p=0.023), BCTQ (p=0.002) and mobility (4 mL: 0.35 [0.58], 2 mL: -0.12 [0.56], and 1 mL: 0.01 [0.39], p=0.04).
Shen YP et al. 2019 RCT China[26]	N=52 20 to 80 years	1, 3 and 6 months	N=26 3 mL 5.0% dextrose	N=26 3 mL platelet rich-plasma	From baseline • Significant improvements in both groups in symptom severity scale, functional status scale and CSA, at each follow-up time-point (p<0.05). Between-groups • Platelet rich-plasma outperformed dextrose in functional status scale at 3 months (p=0.044), distal motor latency at 6 months (p=0.028) and CSA of the median nerve at 3 (p=0.001) and 6 months (p=0.018).
Wu YT et al. 2017 RCT Taiwan[27]	N=49; 60 wrists 58.47±2.33 in dextrose group, 58.10±1.93 in control group	1, 3 and 6 months	N=30 wrists 5 mL 5.0% dextrose	N=30 wrists 5 mL normal saline	Between-groups (as compared to control) • Significant improvements in the VAS at 1-month (p=0.001), 3-month (p=0.02) and 6-month (p<0.001). • Significant improvements in the BCTQ severity scores at 1-month (p=0.02), 3-month (p=0.01) and 6-month (p<0.001). • Significant improvements in the BCTQ function scores at each follow-up time-point (p<0.001).
Lower limbs					
Fu Y et al. 2024 RCT China[28]	N=60 48 to 80 years Knee osteoarthritis	2, 4 and 8 weeks	N=20 2 mL 5.0% dextrose	N=20 Prolotherapy; 8 mL 20.0 dextrose N=20 5.0% dextrose + prolotherapy	Between-groups • After 2 weeks, the VAS and WOMAC scores of the dextrose group and combination groups were significantly lower than prolotherapy group (p<0.05). • After 8 weeks, only the combination group demonstrated significantly lower VAS and WOMAC, and higher pressure pain threshold as compared to other two groups (p<0.05).
Garcia-Triana SA et al. 2020 RCT Mexico[15]	N=50; 99 knees 25 to 70 years Chondro-malacia patella	6 months	N=25; 49 knees 0.5 to 1 mL 5.0% dextrose + home physical therapy	N=25; 50 knees Home physical therapy	Between-groups • The treatment group outperformed the control group in WOMAC (p<0.001) and VAS (p<0.001) after interventions.
Alyan II et al. 2018 RCT Egypt[29]	N=100 40 to 70 years Chronic knee osteoarthritis		N=50 0.5 mL 5.0% dextrose	N=50 Low level laser therapy	Between-groups • The VAS (p<0.001) and WOMAC (p<0.0001) scores significantly improved in the dextrose group.
Guzel I et al. 2021 Retrospective Turkey[30]	N=60 40 to 90 years Total knee arthroplasty	1, 3 and 6 months	N=31 3 mL 5.0% dextrose + standard post-operative care	N=29 Standard post-operative care	Within group • Significant improvements (p<0.001) were observed in both groups regarding on WOMAC and VAS scores. Between-groups • The treatment group were significantly higher than the control group (p<0.001) at at each follow-up time-point.

Other neuropathic pain sites					
Chen LC et al. 2020 RCT Taiwan[31]	N=36 20 to 80 years Ulnar neuropathy	1, 3, 4 and 6 months	N=18 5 mL 5.0% dextrose	N=18 3 mL triamcinolone acetonide 10 mg/mL + 2 mL normal saline	From baseline • VAS and CSA showed significant improvements in both groups at each follow-up time-point (p<0.05).
Maniquis-Smigel G et al. 2017 RCT Hawaii[32]	N=35 19 to 75 years Chronic low back pain	15 minutes, 2, 4, 48 hours and 2 weeks	N=19 10 mL 5.0% dextrose	N=16 10 mL normal saline	Between-groups • The dextrose group had a greater rate of experiencing more than 50.0% reduction in pain after 4 hours (16/19; 84.0%) compared to saline group (3/16; 19.0%; p<0.001).
Kim H et al. 2024 Retrospective South Korea[1]	N=112 40 to 72 years Neuropathic pain (PHN=26, TN=18, CRPS=28, PN=40)	2 weeks	N=89 0.5 to 3 mL 5.0% dextrose	N=23 0.5 to 3 mL 0.5% lidocaine	From baseline • The numerical rating scale pain score decreased significantly in dextrose group in patients with PHN (p<0.01), TN (p<0.05) and PN (p<0.01), but not in CRPS.
Uslu EY 2024 Retrospective Turkey[33]	N=33 18 to 60 years Superior cluneal nerve neuropathy	1 week	N=16 5 mL 5.0% dextrose	N=17 2.63 mg betamethasone sodium phosphate + 5 mg betamethasone dipropionate	Between-groups • After 1 week, the dextrose group outperformed steroid group in VAS (p=0.016) and RMDQ (p=0.009).

RCT, randomised controlled trial; VAS, visual analogue scale; Boston Carpal Tunnel Syndrome Questionnaire; CSA, cross-sectional area; WOMAC, Western Ontario McMaster University Osteoarthritis Index; PHN, postherpetic neuralgia; TN, trigeminal neuralgia; CRPS, complex regional pain syndrome; PN, peripheral neuropathy; RMDQ, Rolland-Morris Disability Questionnaire

SAFETY

There were six studies reported on the safety of perineural 5.0% dextrose injection therapy in treating neuropathic pain.

The safety assessment found that perineural 5.0% dextrose injection therapy was generally safe and had a low frequency of minor adverse events. Overall, research found that during the sessions nor the follow-up sessions, the therapy was linked to any additional conservative therapies or medications.[1,15,26,27,28,31]

COST-EFFECTIVENESS

There was no evidence retrieved on cost-effectiveness or other aspects of the economic implication associated with perineural 5.0% dextrose injection therapy for neuropathic pain. However, the cost per injection is aroun[redacted]; December 2024).[34]

CONCLUSION

There were moderate to high quality evidence showed that perineural 5.0% dextrose injection therapy provides a safe, minimally invasive and effective in improving pain, nerve function and patient-reported outcomes across various conditions, with benefits often exceeding those of saline or corticosteroids. Combined therapies were shown to enhance efficacy for certain conditions in neuropathic pain.

REFERENCE

1. Kim H, Kim HJ, Jung YH et al. The effect of perineural injection therapy on neuropathic pain: a retrospective study. J Dent Anesth Pain Med. 2024; 24(1): 47-56. Doi: https://doi.org/10.17245/jdapm.2024.24.1.47.
2. van Hecke O, Austin SK, Khan RA et al. Neuropathic Pain in the General Population: A Systematic Review of Epidemiological Studies. PAIN. 2014; 155: 654-662.
3. Abbott CA, Malik RA, Van Ross ERE ET AL. Prevalence and Characteristics of Painful Diabetic Neuropathy in a Large Community-based Diabetic Population in the U.K. Diabetes Care. 2011; 34: 2220-2224.
4. Aslam A, Singh J and Rajbhandari S. Prevalence of Painful Diabetic Neuropathy Using the Self-completed Leeds Assessment of Neuropathic Symptoms and Signs Questionnaire in a Population with Diabetes. Can J Diabetes 2015; 39: 285-295.
5. Bouhassira D, Letanoux M and Hartemann A. Chronic Pain with Neuropathic Characteristics in Diabetic Patients: A French Cross-sectional Study. PLoS One. 2013; 8:e74195.
6. Davies M, Brophy S, Williams R et al. The Prevalence, Severity, and Impact of Painful Diabetic Peripheral Neuropathy in Type 2 Diabetes. Diabetes Care. 2006; 29: 1518-1522.
7. Kew Y, Tan CY, Ng CJ et al. Prevalence and Associations of Neuropathic Pain in a Cohort of Multi-ethnic Asian Low Back Pain Patients. Rheumatol Int. 2017; 37(4): 633-639. Doi: 10.1007/s00296-016-3633-x.
8. Park HJ and Moon DE. Pharmacologic Management Of Chronic Pain. Korean J Pain. 2010; 23: 99-108.
9. Riediger C, Schuster T, Barlinn K et al. Adverse Effects of Antidepressants for Chronic Pain: A Systematic Review and Meta-analysis. Front Neurol. 2017; 8: 307.
10. Mondelli M, Filippou G, Frediani B et al. Ultrasonography in Ulnar Neuropathy at the Elbow: Relationships to Clinical and Electrophysiological Findings. Neurophysiol Clin 2008; 38: 217-226.
11. Wu YT, Ke MJ, Ho TY, Li TY, Shen YP, Chen LC. Randomized double-blinded clinical trial of 5% dextrose versus triamcinolone injection for carpal tunnel syndrome patients. Ann Neurol 2018;84: 601-10.
12. Management of Neuropathic Pain (Second Edition). Malaysian Association for the Study of Pain. 2012. Available at https://www.masp.org.my/index.cfm?menuid=21. Accessed on 28 November 2024.
13. Lyftogt J. Subcutaneous Prolotherapy for Achilles Tendinopathy: The Best Solution? Australasian Musculoskeletal Medicine. 2007; 12: 107-109.
14. Wu YT, Chen YP, Lam KHS et al. Mechanism of Glucose Water as a Neural Injection: A Perspective on Neuroinflammation. Life. 2022; DOI: https:// doi. org/10. 3390/ life1 20608 32.
15. Garcia-Triana SA, Toro-Sashida MF, Larios-Gonzalez XV et al. The Benefit of Perineural Injection Treatment with Dextrose for Treatment of Chondromalacia Patella in Participants Receiving Home Physical Therapy: A Pilot Randomized Clinical Trial. J Altern Complement Med. 2020; 0(0): 1-7. Doi: 10.1089/acm.2020.0287.
16. Lam KHS, Hung CY, Chiang YP et al. Ultrasound-guided Nerve Hydrodissection for Pain Management: Rationale, Methods, Current Literature, and Theoretical Mechanisms. J. Pain Res. 2020; 13: 1957-1968.
17. Lam KHS, Hung CY, Chiang YP et al. Practical Considerations for Ultrasound-guided Hydrodissection in Pronator Teres Syndrome. Pain Med. 2022; 23: 221-223.
18. Lam SKH, Reeves KD and Cheng AL. Transition from Deep Regional Blocks Toward Deep Nerve Hydrodissection in the Upper Body and Torso: Method Description and Results from a Retrospective Chart Review of Tthe Analgesic Effect of 5% Dextrose Water as the Primary Hydrodissection Injectate to Enhance Safety. BioMed Res. Int. 2017. 2017; 7920438.
19. Wu YT, Chen SR, Li TY et al. Nerve Hydrodissection for Carpal Tunnel Syndrome: A Prospective, Randomized, Double-blind, Controlled Trial. Muscle Nerve. 2019; 59: 174-180.
20. Hung CY, Lam KHS, Wu YT. Dynamic Ultrasound for Carpal Tunnel Syndrome Caused by Squeezed Median Nerve between the Flexor Pollicis Longus and Flexor Digitorum Tendons. Pain Med. 2021; Online ahead of print.
21. MacIver MB and Tanelian DL. Activation of C fibers by Metabolic Perturbations Associated with Tourniquet Ischemia. Anesthesiology. 1992; 76: 617-623.
22. Jensen VF, Mølck AM, Bøgh IB et al. Effect of Insulin-induced Hypoglycaemia on the Peripheral Nervous System: Focus on Adaptive Mechanisms, Pathogenesis and Histopathological Changes. J. Neuroendocrinol. 2014; 26: 482-496.
23. Lyftogt Perineural Injection Treatment™ (LPIT) – Neurofascial Prolotherapy. Available at https://caringmedical.com/prolotherapy-news/lyftogt-perineural-injection-treatment/. Accessed on 2 December 2024.
24. Your Guide to Perineural Injection Therapy. Available at https://www.empiremedicaltraining.com/blog/your-guide-to-perineural-injection-therapy/#:~:text=How%20Does%20Perineural%20Injection%20Therapy,over%20a%20period%20of%20months. Accessed on 2 December 2024.
25. Lin MT, Liu IC, Syu WT et al. Effect of Perineural Injection with Different Dextrose Volumes on Median Nerve Size, Elasticity and Mobility in Hands with Carpal Tunnel Syndrome. Diagnostics. 2021; 11: 849. DOI: https://doi.org/10.3390/diagnostics11050849.

26. Shen YP, Li TY, Chou YC et al. Comparison of Perineural Platelet-rich Plasma and Dextrose Injections for Moderate Carpal Tunnel Syndrome: A Prospective Randomized, Single-blind, Head-to-head Comparative Trial. J Tissue Eng Regen Med. 2019; DOI: https://doi.org/10.1002/term.2950.
27. Wu YT, Ho TY, Chou YC et al. Six-month Efficacy of Perineural Dextrose for Carpal Tunnel Syndrome: A Prospective, Randomized, Double-blind, Controlled Trial. Mayo Clin Proc. 2017; 92: 1179-1189.
28. Fu Y, Du Y, Li J et al. Demonstrating the Effectiveness of Intra-articular Prolotherapy Combined with Peri-articular Perineural Injection in Knee Osteoarthritis: A Randomized Controlled Trial. Journal of Orthopaedic Surgery and Research. 2024; 19: 279. DOI: https://doi.org/10.1186/s13018-024-04762-4.
29. Alyan II and El-Rouby MA. Comparison of Analgesic Effect of Perineural Dextrose Injection and Low Level Laser Therapy for Osteoarthritis Knee Pain. Med. J. Cairo Univ. 2018; 86(5): 2727-2731.
30. Guzel I, Gul D, Akpancar S et al. Effectiveness of Perineural Injections Combined with Standard Postoperative Total Knee Arthroplasty Protocols in the Management of Chronic Postsurgical Pain After Total Knee Arthroplasty. Med Sci Monit. 2021; 27: e928759. DOI: 10.12659/MSM.928759.
31. Chen LC, Ho TY, Shen YP et al. Perineural Dextrose and Corticosteroid Injections for Ulnar Neuropathy at the Elbow: A Randomized Double-blind Trial. ACRM. 2020; 101: 1296-1303.
32. Maniquis-Smigel L, Reeves KD, Rosen HJ et al. Short Term Analgesic Effects of 5% Dextrose Epidural Injections for Chronic Low Back Pain: A Randomized Controlled Trial. Anesth Pain Med. 2017; 7(1): e42550.
33. Uslu EY. Ultrasound-guided Perineural Dextrose Injection for Superior Cluneal Nerve Neuropathy Treatment. Cureus. 2024; 16(9): e70229. DOI: 10.7759/cureus.70229.
34. Pricing and Payment for Lyftogt Perineural injections / Neurofascial Prolotherapy. Available at https://caringmedical.com/for-patients/pricing-and-payment-policies/. Accessed on 3 December 2024.

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