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Efficacy of neural prolotherapy in treatment of meralgia paresthetica: a case series

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Abstract

Background: Meralgia paresthetica is an entrapment neuropathy. Neuropathic pain was reported to be improved by using neural prolotherapy. Aim of the research was to assess and evaluate the short-term efficacy of neural prolotherapy on relieving pain, paresthesia and improving function and quality of life of patients with meralgia paresthetica. The study included 19 lower limbs with idiopathic meralgia paresthetica obtained from 15 patients. Subcutaneous perineural injection of dextrose (5%) in sterile water was given once. All patients were evaluated for outcome measures twice, at baseline visit and at follow-up visit four weeks after the injection which included: patient assessment of overall symptoms of meralgia paresthetica, patient assessment of meralgia paresthetica pain, patient assessment of meralgia paresthetica paresthesia and patient assessment of meralgia paresthetica effect on function and quality of life using visual analogue scale.

Results: There was a statistically significant improvement in the visual analogue scale of patient assessment of overall meralgia paresthetica symptoms, patient assessment of meralgia paresthetica pain, patient assessment of meralgia paresthetica paresthesia and patient assessment of meralgia paresthetica effect on function and quality of life when the findings at the postinjection visit were compared to the preinjection assessment among all patients. All the patients tolerated the injection procedure-induced pain. All the patients experienced immediate postinjection relieve of the meralgia paresthetica pain. At the postinjection assessment visit, all patients were satisfied with the procedure. There were 12 lower limbs (63.2%) from 10 patients (66.6%) that showed improvement and recovery. Two patients of them had bilateral meralgia paresthetica. There was no patient withdrawal, and no patients were lost to follow-up. There was one lower limb (5.3%) from one patient (6.7%) who had bruises at the injection sites that resolved within few days after the procedure.

Conclusions: Neural prolotherapy is easy, safe, tolerable, effective and successful in treatment of meralgia paresthetica. It is effective in relieving pain, paresthesia and improving function and quality of life of patients with meralgia paresthetica. Neural prolotherapy injection should be included in the conservative treatment armamentarium of meralgia paresthetica.

Trial registration : NCT04499911. Registered 5 August 2020—retrospectively registered.

Keywords: Lateral cutaneous nerve of the thigh, Lateral femoral cutaneous nerve, Lateral femoral cutaneous nerve entrapment neuropathy, Meralgia paresthetica, Subcutaneous perineural injection, Neural prolotherapy, Prolotherapy, Pain treatment

Background

Meralgia paresthetica (MP) is a neuropathy of the lateral

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femoral cutaneous nerve (LFCN) (i.e., lateral cutaneous nerve of the thigh). It is known as the lateral cutaneous nerve of the thigh neuralgia [1]. It is usually an entrapment neuropathy of the LFCN [2–4]. MP is characterized by pain, tingling, paresthesia and numbness in the anterolateral aspect of the thigh. The symptoms may be participated or increased by prolonged standing and walking. Sitting may alleviate the pain because there is reduction of the tension over the nerve [1, 2, 5].

The treatment of MP is directed towards the improvement of the symptoms which is mainly pain with subsequent improvement of function and quality of life (QoL), as well as, treatment of the etiology. It includes conservative treatment and surgical intervention. Conservative treatment consists of non-pharmacologic treatment and pharmacologic treatment [1, 2, 5–9]. Surgical treatment is indicated in case of failure of conservative treatment. Surgical options consist of neurolysis and neurectomy [10].

Neural prolotherapy (NP) was reported to improve and relieve neuropathic pain [11, 12]. NP is the subcutaneous perineural injection of isotonic dextrose 5% in sterile water (D5W) solution especially at the points of fascial penetration of the sensory nerve. It is the site where the sensory nerve reaches the subcutaneous plane [11–13].

There are scanty studies that assessed the efficacy of NP in improving and relieving neuropathic pain [11, 12]. Also, there are no previous studies in the literature that assessed the efficacy of NP in the treatment of MP. Aim of the research was to assess and evaluate the short-term efficacy of NP (subcutaneous perineural injection of D5W solution) on relieving pain, paresthesia and improving function and QoL of patients with MP.

Methods

Study design and ethics statement

The current study was a single-center prospective case series study. The researcher explained the study for all the participants, and each one gave an informed consent. The local Institutional Ethics Committee approved the study. The study was registered in the ClinicalTrials.gov (a trial registry) with an identifier number of NCT04499911.

Study participants and patient selection

Twenty patients were recruited sequentially from those attending the Physical Medicine, Rheumatology and Rehabilitation outpatient clinic of Main University Hospital (a single tertiary referral academic medical center), Alexandria University Faculty of Medicine, Alexandria Governorate, Egypt, between April 2018 and September 2019.

The clinical diagnosis of MP was based on the following: (i) the presence of pain, paresthesia and numbness over the anterior and lateral aspect of the thigh; (ii) exacerbation of these symptoms on walking, standing and hip extension; and (iii) MP was confirmed electrophysiologically by nerve conduction study with or without somatosensory evoked potential [14]. The MP symptoms needed to be present for at least three months. Participants were unresponsive to conservative treatment. The conservative treatment included lifestyle modification including activity modification (avoid the use of seat belts) and avoidance of tight underwear (tight garments such as jeans and uniforms); weight reduction; non-steroidal anti-inflammatory drugs and anticonvulsants for neuropathic pain; and physiotherapy.[1, 2, 7] Exclusion criteria included diabetes mellitus, endocrine disorders, metabolic disorders, systemic rheumatologic disorders, neurological disorders including peripheral neuropathy, lumbar radiculopathy and lumbar plexopathy; coagulopathy, anticoagulant treatment, current skin or soft tissue infection at or near the site of injection, prior local injection of corticosteroid in the past year for MP, prior NP in the past year for MP, prior surgery in the affected thigh region, patients presented with a systemic active inflammatory condition or infection, and pregnancy.

After screening, 15 patients were selected for the study. Four patients had exclusion criteria (three patients had diabetes mellitus and one patient received anticoagulant treatment) and one patient refused to participate in the study. A total of 19 lower limbs with idiopathic MP obtained from 15 patients were included in the current study (Fig. 1).

Study assessment

All patients involved in the study were assessed as the following: demographic data collection including age and sex. Body mass index (BMI) was assessed (weight [kg]/[height (m)]^2) [15]. Clinical examination was done including neurological and musculoskeletal examination.

Study intervention

Patients included in the study received subcutaneous perineural injection of D5W solution [11, 13]. Before injection, clinical examination of the thigh was done to detect tender points along the anatomical course of the LFCN which start from the LFCN fascial penetration point. It is located at the crossing point of the line drawn directly down from the anterior superior iliac spine (ASIS) and the line level with the lower border of the symphysis pubis, in the depression on the lateral side of the sartorius muscle when the thigh is flexed. Then, all tender points along the course of the LFCN distally are identified. They are usually located along a line extending from the ASIS to a point on the lateral end of the

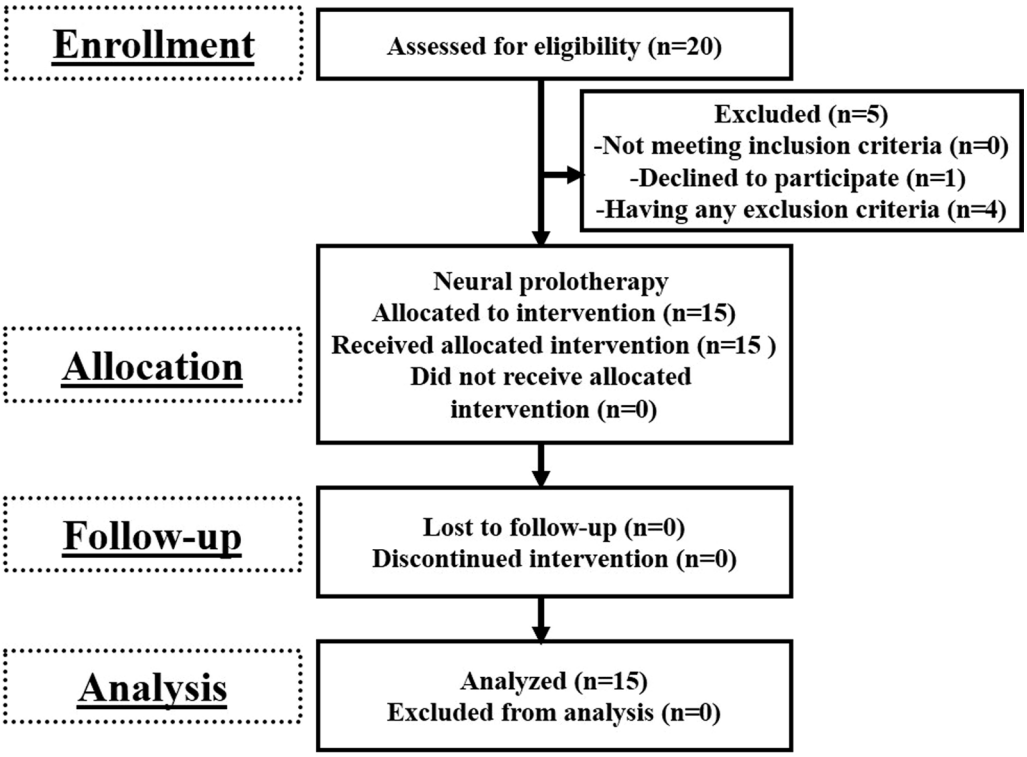

Fig. 1 The study flowchart. *n*, number of patients

superior border of the patella. The end of the course is about four finger breaths proximal to the patella [13]. The tender points were marked. Patient feedback was used to localize the tender points.

The injection procedure was done while the patient lying supine and fully extending the hips and knees. The anterolateral aspect of the thigh with identified tender points (i.e., injection area) was sterilized with povidone-iodine solution then with medical alcohol (70%). Injection was done through an aseptic technique to minimize risk of infection. Subcutaneous injection of D5W solution was done using a 28-gauge needle (length: 12.75 mm) and an insulin syringe. D5W solution was available as container of 250 ml. The D5W solution was withdrawn from the D5W solution container by using a 23-gauge needle. The injection was done starting from the LFCN fascial penetration point. All tender points were injected with D5W solution. Each tender point was injected with 0.5 ml of D5W solution subcutaneously about 0.5 cm deep. A skin bleb was formed with injected solution [11, 13]. Up to 10 skin punctures were done, placing a minimal total volume of 5 ml of D5W solution. After that, the patient was asked to point to any painful and tender points left without injection. These points were subsequently injected by the same procedure. The aim was to achieve complete relief of pain at the end of injection procedure. The injection procedure was completed once all tender points were injected [11, 13].

Immediately following the end of injection procedure, the patient was asked to assess the injection procedure-induced pain by visual analogue scale (VAS) (a 10-cm horizontal scale) in which it ranged from 0 (no pain) to 10 (severe intolerable pain) [16]. Also, immediately postinjection assessment of MP pain severity was assessed by VAS (a 10-cm horizontal scale) in which it ranged from 0 (no pain) to 10 (severe intolerable pain) [16].

Rescue medication and postinjection care

The patients were instructed to stop all analgesics 48 h before the procedure and for a period of 4 weeks after the injection. After injection, instructions regarding resting the thigh for 24 h were given. Only acetaminophen was recommended occasionally to control intolerable thigh pain (taken orally and up to 4 g per day was allowed) and discontinued 48 h prior to the postinjection visit. All patients were instructed for weight reduction and wearing looser fitting clothes. Instruction for the patients was given that injection could be repeated at one week if their

pain and symptoms recurred within one week from the initial injection.

Study schedule and outcome measures

All patients were evaluated for outcome measures twice (Fig. 1). Initial baseline assessment was done before injection (preinjection assessment). Reassessment was done after injection by four weeks (postinjection assessment). The assessment included: (I) primary outcome measure: patient assessment of overall symptoms of MP. It was evaluated collectively by using VAS (a 10-cm horizontal scale) which ranged from 0 (no MP symptoms) to 10 (severe intolerable symptoms) [16]. Secondary outcome measures: (i) patient assessment of MP pain. It was evaluated by using VAS which ranged from 0 (no pain) to 10 (severe intolerable pain); (ii) patient assessment of MP paresthesia. It was evaluated by using VAS which ranged from 0 (no paresthesia) to 10 (severe intolerable paresthesia); (iii) patient assessment of the effect of MP symptoms on function and QoL. It was evaluated by using VAS which ranged from 0 (no influence on QoL) to 10 (severe influence on QoL) [16–18].These assessment methods have good validity and excellent reliability [17, 18]. Only in the postinjection visit the patient's degree of satisfaction regarding the procedure results was assessed by using a VAS which ranged from 0 (no satisfaction at all), to 10 (complete satisfaction) [16]. Searching for side effects of NP and recurrence of symptoms were done in the postinjection assessment visit.

According to the results of the outcome measures in the four-week postinjection assessment, the patients were categorized as having the following [19].

(I) Complete recovery of MP: The patient had no pain, no symptom and complete recovery of their function and QoL.
(II) Partial recovery of MP: There was no complete recovery but the patient had improvement of more than 50% in the primary outcome measure and any of the secondary outcome measures.
(III) No recovery of MP: The patient had no improvement of more than 50% in the primary outcome measure and any of the secondary outcome measures.

Statistical assessment of data was performed using the SPSS (version 17) software. The following constituted the descriptive measures (count, frequency, minimum, maximum, median, mean and standard deviation [SD]). The following constituted the analytic measures: (i) qualitative data were analyzed using Chi-square test or Fisher's exact test (when required) and (ii) quantitative data were analyzed using Mann–Whitney test and Wilcoxon signed ranks test. Statistical significance difference was considered for any P value less than 0.05.

Results

The study included 19 lower limbs obtained from 15 patients with MP. There were 11 women (73.3%). The mean age of the patients was 41.66 ± 11.16 years (ranged from 22 to 59 years). The characteristics of the patients are summarized in Table 1. There were four patients (26.7%) with bilateral MP.

There was a statistically significant improvement in the VAS of patient assessment of overall MP symptoms, patient assessment of MP pain, patient assessment of MP paresthesia and patient assessment of MP effect on function and QoL when the findings at the postinjection visit were compared to the preinjection assessment among all patients. All the patients tolerated the injection procedure-induced pain. All the patients experienced immediate postinjection relief of the MP pain (Table 2). At the postinjection assessment visit all patients were satisfied with the procedure.

Regarding the effectiveness of the intervention, 12 lower limbs (63.2%) from 10 patients (66.6%) showed improvement and recovery. Two patient (20%) of them had bilateral MP. In each one, complete improvement was present in one lower limb and partial improvement occurred in the other lower limb. These constituted the

Table 1 Demographic, anthropometric and clinical characteristics of the patients

Demographic, anthropometric and clinical characteristics of the patients	Patient group ($n = 19$ lower limbs from 15 patients)§	Range
Age (year)*	43(41.66 ± 11.16)	22 to 59
Women†	11(73.3)	NA
Weight (kg)*	90(88.31 ± 16.15)	61 to 119
Height (cm)*	162(162.94 ± 6.24)	150.00 to 173.50
BMI (kg/m^2)*	33.46(33.17 ± 5.23)	22.05 to 43.70
BMI categories		
Normal weight†	1(6.7)	NA
Overweight†	3(20)	NA
Obesity†	10(66.6)	NA
Morbid obesity†	1(6.7)	NA
Side (right/left)‡	10/9(52.6/47.4)	NA
Duration of the symptoms (months)*	12(14.47 ± 9.31)	4 to 36

kg kilogram; *cm* centimeter; *BMI* body mass index; *m* meter; *n* number of lower limbs; *NA* not applicable

* Data are reported as median (mean ± standard deviation)

† Data are reported as number (percentage) of patients

‡ Data are reported as number (percentage) of lower limbs

§ There were four patients with bilateral meralgia paresthetica

Table 2 Comparison between the preinjection and the postinjection assessments regarding outcomes measures and procedure assessment

Outcomes measures	Preinjection assessment ($n=19$ lower limbs from 15 patients)§	Postinjection assessment ($n=19$ lower limbs from 15 patients)§	Test of significance‖	*P*
Overall MP symptoms (VAS)†	7(7.00 ± 1.49)	1(1.84 ± 1.80)	-3.848	≤ 0.0001*
MP pain (VAS)†	6(6.42 ± 1.92)	1(1.94 ± 1.87)	-3.745	≤ 0.0001*
MP paresthesia (VAS)†	7(7.31 ± 1.49)	1(1.89 ± 2.13)	-3.835	≤ 0.0001*
MP effect on function and QoL (VAS)†	5(5.57 ± 1.67)	0(1.05 ± 1.47)	-3.839	≤ 0.0001*
Procedure assessment				
Immediately postinjection MP pain (VAS)†	0(0)	NA	NA	NA
Injection procedure-induced pain (VAS)†	2.5(2.44 ± 0.81)	NA	NA	NA
Presence of injection procedure side effects‡	NA	1(5.3)	NA	NA
Degree of satisfaction regarding the procedure (VAS)†	NA	8(7.42 ± 2.75)	NA	NA

MP meralgia paresthetica; *VAS* visual analogue scale; overall MP symptoms; patient assessment of overall MP symptoms; MP pain; patient assessment of MP pain; MP paresthesia; patient assessment of MP paresthesia; *QoL* quality of life; MP effect on function and QoL; patient assessment of MP effect on function and QoL; *n* number of lower limbs; *NA* not applicable

* *P* is significant at < 0.05

† Data are reported as median (mean ± standard deviation)

‡ Data are reported as number (percentage) of lower limbs

§ There were four patients with bilateral meralgia paresthetica

‖Value of Wilcoxon Signed Ranks test

improved patients group. Among them, six lower limbs (50%) from six patients (60%) had complete recovery of MP while another six lower limbs (50%) from six patients (60%) had partial recovery of MP. No recovery was present in seven lower limbs (36.8%) obtained from five patients (33.4%). These constituted the non-improved patients group.

There was no patient withdrawal, and no patients were lost to follow-up. One lower limb (5.3%) from one patient (6.7%) had bruises at the injection sites that resolved within few days after the procedure. Other than that, there were no drug and procedure side effects reported by the patients in the four-week postinjection follow-up visit.

Table 3 shows the comparison between the improved patients group versus non-improved patients group regarding the demographic, anthropometric and clinical characteristics; preinjection outcomes measures and procedure assessment. There was a statistically significant difference between both groups regarding the patient assessment of MP pain using VAS which was significantly higher among the non-improved patients group ($P=0.028$). There was a statistically significant difference between both groups regarding the degree of satisfaction to the procedure which was significantly higher among the improved patients group versus the non-improved patients group ($P\leq 0.0001$) (Table 3).

Only five lower limbs (26.3%) of four patients (26.7%) received a NP extra-injection upon their request due to inadequate improvement within the first week after injection. Among them, there were four lower limbs (80.0%) of three patients (75%) within the non-improved group of patients. The percentage of patients who needed NP extra-injection was statistically significantly higher among the non-improved patients group in comparison with the improved patients group ($P=0.038$) (Table 3).

Discussion

Lateral femoral cutaneous nerve is a sensory nerve. Its nerve roots are the second and third lumbar spinal nerves. It is a branch of lumbar plexus. It appears from the lateral border of the psoas major muscle. It crosses superficial to the fascia of the iliacus muscle. Then it runs just deep to the inguinal ligament [20]. In most of the subjects, LFCN passes under the inguinal ligament medial to the medial tip of the ASIS [21]. However, LFCN has some anatomical variations in relation to the ASIS. Some of them make the individuals more prone to develop MP than others [1]. Then LFCN pierces the deep fascia inferior to the inguinal ligament usually at a point about 2–3 cm distal to the ASIS. Then it runs laterally and distally within the subcutaneous tissue of the anterolateral aspect of the thigh where it is divided into two terminal braches (i.e., the anterior and posterior branches) [22, 23].

Meralgia paresthetica is a neuropathy of the LFCN. It is usually an entrapment neuropathy of the LFCN when it passes deep the inguinal ligament to enter the thigh

Table 3 Comparison between the improved patients group versus non-improved patients group regarding different assessed parameters

Demographic, anthropometric and clinical characteristics; preinjection outcomes measures and procedure assessment	Improved patients group (*n* = 12 lower limbs from 10 patients)‖	Non-improved patients group (*n* = 7 lower limbs from 5 patients)¶	Test of significance	*P*
Age (year)†	44.50(43.75 ± 10.69)	39(38.42 ± 9.03)	(Z) − 1.016	0.340
Women‡	7(70)	4(80)	(X^2) 0.170	0.680
Weight (kg)†	93.25(90.37 ± 18.20)	78.00(84.78 ± 12.34)	(Z) − 0.931	0.352
Height (cm)†	161(162.25 ± 7.27)	164(164.14 ± 4.18)	(Z) − 0.764	0.445
BMI (kg/m^2)†	34.66(34.19 ± 5.76)	31.24 (31.42 ± 3.94)	(Z) − 1.270	0.204
BMI categories				
Normal weight‡	1(10)	0(0)	(X^2) 2.550	0.466
Overweight‡	1(10)	2(40)		
Obesity‡	7(70)	3(60)		
Morbid obesity‡	1(10)	0(0)		
Side (right/left)§	6/6(50/50)	4/3(57.1/42.9)	(X^2) 0.090	0.764
Duration of the symptoms (months)†	12(14.16 ± 9.55)	12(15.00 ± 9.60)	(Z) − 0.043	0.967
Preinjection outcomes measures				
Overall MP symptoms (VAS)†	7(7.08 ± 1.37)	7(6.85 ± 1.77)	(Z) − 0.476	0.650
MP pain (VAS)†	5(5.75 ± 1.71)	7(7.57 ± 1.81)	(Z) − 2.261	0.028*
MP paresthesia (VAS)†	7(6.91 ± 1.50)	8(8.00 ± 1.29)	(Z) − 1.637	0.120
MP effect on function and QoL (VAS)†	5(5.50 ± 1.78)	6(5.71 ± 1.60)	(Z) − 0.607	0.592
Procedure assessment				
Immediately postinjection MP pain (VAS)†	0(0)	0(0)	(Z) 0.000	1.000
Injection procedure-induced pain (VAS)†	2.75(2.54 ± 0.86)	2(2.28 ± 0.75)	(Z) − 0.709	0.536
Presence of injection procedure side effects§	1(8.3)	0(0)	(X^2) 0.616	0.632#
Receiving an extra-injection upon request§	1(8.3)	4(57.1)	(X^2) 5.432	0.038*#
Degree of satisfaction regarding the procedure (VAS)†	9.50(9.16 ± 1.02)	4(4.42 ± 2.07)	(Z) − 3.448	≤ 0.0001*

kg kilogram; cm, centimeter; *BMI* body mass index; *m* meter; *MP* meralgia paresthetica; *VAS* visual analogue scale; overall MP symptoms; patient assessment of overall MP symptoms; MP pain; patient assessment of MP pain; MP paresthesia; patient assessment of MP paresthesia; *QoL* quality of life; MP effect on function and QoL; patient assessment of MP effect on function and QoL; *n* number of lower limbs

* *P* is significant at < 0.05

† Data are reported as median (mean ± standard deviation)

‡ Data are reported as number (percentage) of patients

§ Data are reported as number (percentage) of lower limbs

‖Bilateral lower limbs with meralgia paresthetica were obtained from two patients (20%) among improved patients group

¶ Bilateral lower limbs with meralgia paresthetica were obtained from two patients (40%) among non-improved patients group

\# *P* value of Fisher's exact test

region. It is usually idiopathic [2]. It is common among obese individuals, pregnant women, patients with increased intra-abdominal pressure and pendulous abdomen with abdomen bulging over the inguinal ligament [24]. This is because of the close relationship between the LFCN and iliac fascia. The protruding abdomen results in traction of the iliac fascia on the LFCN [2, 25]. It could be due to nerve stretching by repetitive motion of the hip joint [2].Direct pressure on the nerve and its subsequent compression can occur by wearing tight underwear, pants, belts, corset and tight low-waist trousers or even tight car seatbelts [2, 3]. These leads to pathological changes in the nerve [10].

The mean age of patients included in the study was 41.66 years. This was in accordance with previous researches [2, 7]. Bilateral MP was present in four patients (26.7%). This was in accordance with previous studies that reported MP to be bilateral in about 20% of the cases [4]. The majority of the patients were obese (66.6%) and one patient (6.7%) was morbid obese. This was in agreement with literature that reported MP to be common among obese patients [2, 7].

There were 12 lower limbs (63.2%) from 10 patients (66.6%) who showed improvement and recovery. This was not assessed previously in the literature. This is considered the first case series study that assessed NP

for the treatment of MP. The effectiveness of NP in this study was comparable with the results of other interventions for MP. Kalichman et al. reported that improvement was present in 60% of their MP patients by using Kinesio taping treatment approach for MP [18]. Elavarasi et al. reported that improvement was present in 75% of their patients with MP by using local injection of triamcinolone acetonide [26]. De Ruiter et al. reported that successful MP improvement was observed more after neurectomy (93.3%) than after neurolysis (37.5%) [10]. The percentage of improvement in the current study was in agreement with a previous study assessed the effect of NP on carpal tunnel syndrome (improvement of 70% of patients) [27].

There was no patient withdrawal, and no patients were lost to follow-up. All the patients tolerated the injection procedure-induced pain. There was one lower limb (5.3%) from one patient (6.7%) who had bruises. All patients were satisfied with the procedure at the postinjection assessment visit. These were in accordance with previous studies that assessed efficacy of NP for carpal tunnel syndrome and other musculoskeletal problems [27–29]. These indicated that NP procedure for MP was a simple, easy, safe and minimally invasive procedure [11, 13, 28–31].

Immediate postinjection disappearance of the MP pain was reported by all patients. This was in agreement with previous studies that reported NP produce quick relief of pain after injection [11, 32].

An extra NP injection was done in five lower limbs (26.3%) from four patients (26.7%). This was done upon the patients request due to inadequate improvement within the first week after NP injection. The majority of them (three patients [75%]) were within the non-improved group of patients. No improvement within the first week after injection and the need for an extra-injection could be an indicator of inadequate efficacy of NP. It was reported that some patients need a large number of NP sessions to show complete improvement of symptoms [30, 33, 34].

To understand the mechanism of action of NP in the treatment of MP, the pathogenesis of MP should be discussed. Compression of the LFCN causes nerve ischemia [35, 36]. When the LFCN is irritated by nerve ischemia, the transient receptor potential vanilloid-1 (TRPV1)-sensitive C pain fibers in the nerve and in the nervi nervosum produce two neuropeptides which are substance P and calcitonin gene-related peptide (CGRP) [11, 32, 35]. These are released from the nociceptors and induce neurogenic inflammation. This cause plasma extravasation, nerve edema and pain [13, 32, 37]. These are due to increase vascular permeability of the blood supply to the nerve. Subsequently, edema formation in the subendoneurial space within the nerve takes place. So, the pressure in the nerve fascicles increases and interferes with the normal endoneurial microcirculation [35, 36]. When the nerve swelling reaches the fascial penetration points, chronic constriction injury (CCI) takes place. The CCI site inhibits the normal neural axoplasmic flow of the nerve growth factors which are essential for nerve integrity and repair [13, 32, 37]. The neurogenic inflammation lowers the firing threshold and induces ectopic activity of the nociceptive neurons and produces neuropathic pain [35]. Subsequently, the treatment of neurogenic inflammation is associated with improvement of neuropathic pain [11, 35].

Neural prolotherapy is the subcutaneous perineural injection of isotonic D5W solution especially at the fascial penetration points of the sensory nerve through which sensory nerve reaches the subcutaneous plane. It was found to produce an immediate analgesic effect following its injection [11–13]. It is a type of prolotherapy [33]. Prolotherapy is the injection of a small quantity of a proliferant solution in specific points at the painful musculoskeletal structure to induce healing process. The most common proliferant solution is dextrose solution [38]. Dextrose is a water soluble, and it is normally present in the blood. It can be injected safely in multiple areas and in any quantities [13, 38].

The mechanism of action of NP using D5W solution is unknown. It was postulated that dextrose inhibits neurogenic inflammation through acting on glucose-responsive nerves. Dextrose 5% inhibits TRPV1 receptor (a capsaicin-sensitive receptor). TRPV1 receptor is a ligand-gated non-selective cation channel that has a role in pain response to stimuli as endogenous lipids, low PH and capsaicin [27, 39]. When TRPV1 receptors are inhibited by dextrose 5%, there is decreasing in the release of proinflammatory neuropeptides as substance P and CGRP which are essential for induction of neurogenic inflammation [11, 32]. The inhibition of TRPV1 receptor by D5W allows resolution of neurogenic inflammation. There is decreasing in nerve swelling, and this allows normal flow of different nerve growth factors. The end result is nerve recovery and decreased pain [32]. It was reported that subcutaneous injection of dextrose in a concentration as little as 0.5% stimulates human cells to start proliferation, increase in cell protein and DNA synthesis. Also, it stimulates the release of a variety of growth factors as platelet-derived growth factor and transforming growth factor-β and other growth factors [40–42]. The use of dextrose solution of concentration below 10% directly stimulates cell proliferation without any inflammatory reactions [13, 38]. This is opposite to the use of dextrose solutions of 10% or more which leads to osmotic gradient outside the cells with subsequent cell lyses that end with

inflammatory cells infiltration with influx of growth factors and induce a sterile inflammatory reaction as wound healing cascade [13, 30].

There was a statistically significant difference between the improved patients group versus the non-improved patients group regarding the preinjection patient assessment of MP pain using VAS which was significantly higher among the non-improved patients ($P=0.028$). The higher the patient assessment of MP pain severity could be an indicator of failure of NP injection for MP. Patients with high pain severity could have more severe intraneural changes within the LFCN which becomes irreversible [10]. Also, the percentage of patients needed NP extra-injection was statistically significantly higher among the non-improved patients group in comparison with the improved patients group ($P=0.038$). The need for an extra-injection of NP could be an indicator of failure of NP injection for MP.

Limitations of the research: (i) This was a case series study without a control group. Ethically, it was not acceptable to do an invasive maneuver using a placebo drug to patients with MP. All recruited patients were unresponsive to conservative therapy. Spontaneous improvement of the improved patients was unlikely. A placebo effect may explain the improvement partially. (ii) There is no standardized protocol for the number of NP sessions and their schedule for MP. There is no standardization for the dosage of D5W solution. The optimal number and schedule of sessions, as well as the optimal dosage, are still unknown. Future researches are recommended to clarify and explore these items. (iii) The mechanism of action of NP using D5W solution was not evaluated in the current study. Future studies are needed to evaluate the mechanism of action of NP. (iv) The small number of patients included in the current study. This was due to: (a) the inclusion of chronic patients having MP for at least three months who were unresponsive to conservative treatment. Treatment of MP involves a stepwise approach and about 85% of MP patients are effectively improved by conservative treatment, but only 15% of patients remain refractory [43]; (b) the wide range of exclusion criteria presented in the current study; (c) patients with chronic MP who were unresponsive to conservative treatment preferred to seek neurosurgery consultation and not physical medicine, rheumatology and rehabilitation consultation; and (d) the low incidence of MP which was estimated at approximately 4.3 per 10,000 person per year [2]. Further studies with a larger sample size are recommended. (v) The study did not assess the long-term effect of NP. A longer follow-up period is recommended to evaluate the long-term efficacy of NP. (vi) The study was conducted in a single medical center. Subsequently, the generalization of the obtained results needs to be taken cautiously.

Conclusions

In conclusion, NP is easy, safe, tolerable, effective and successful in treatment of MP. NP is effective on relieving pain, paresthesia and improving function and QoL of patients with MP. NP injection should be included in the conservative treatment armamentarium of MP. Further multi-center randomized placebo controlled studies should be done on a larger number of patients for verification the effectiveness of NP in the treatment of MP. A longer follow-up period is recommended to evaluate the long-term efficacy of NP.

Abbreviations

ASIS: Anterior superior iliac spine; BMI: Body mass index; CCI: Chronic constriction injury; CGRP: Calcitonin gene-related peptide; D5W: Dextrose 5% in sterile water; LFCN: Lateral femoral cutaneous nerve; MP: Meralgia paresthetica; NP: Neural prolotherapy; QoL: Quality of life; SD: Standard deviation; TRPV1: Transient receptor potential vanilloid-1; VAS: Visual analogue scale.

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Author contributions

The author (EKAS) contributed in the concepts, design, definition of intellectual content, literature search, clinical studies, data acquisition and analysis, manuscript preparation, editing and revision. The author approved the manuscript. The author read and approved the final manuscript.

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Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The local Ethics Committee of Faculty of Medicine, Alexandria University, Egypt (IRB NO: 00007555-FWA NO: 00018699), approved the study. Date of approval: 12/4/2018. Serial number: 0303901.

Informed consent

A written informed consent was given by each participant.

Consent for publication

Consent for publication was given by each participant.

Competing interests

The author declares that he has no competing interests.

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