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Original Article

Percutaneous Pulsed Radiofrequency versus Combined Intradiscal Oxygen-Ozone Therapy with Percutaneous Radiofrequency for Management of Discogenic Cervical Radiculopathy

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BACKGROUND: Cervical radiculopathy can lead to severe disability. Non-invasive treatment can be the primary option in many circumstances. Minimally invasive therapies were developed to provide good clinical results while also being a low-cost technique that is well tolerated. These methods have gained popularity in recent years as it avoids severe soft-tissue injury, extensive hospitalization, and a lengthy recovery period. Radiofrequency (RF) is classified into continuous radiofrequency, which uses thermocoagulation, and pulsed radiofrequency (PRF), which uses an electromagnetic field.

OBJECTIVE: The aim of this study was to compare between PRF at the cervical root combined with intradiscal ozone injection and PRF alone for treatment of patients with discogenic cervical radiculopathy.

PATIENTS AND METHODS: The present study was carried out at Neurosurgery department, Alexandria University on 60 patients with cervical radiculopathy in a randomized controlled clinical trial. Patients were randomly allocated by a computer based program into three groups (20 patients each). In group I patients had PRF combined with intradiscal oxygen-ozone, in group II patients had PRF alone, and in group III, the control group, patients received only diagnostic blocks.

RESULTS: Our study showed that PRF combined with intradiscal ozone and pulsed RF alone had good clinical outcome when comparing it to control group in terms of reduction of pain, need of medications, neck disability index and need for surgery. There was significant shrinkage of herniated disc fragment in magnetic resonance imaging (MRI) done 3 months after intervention in 5 patients in Group I.

CONCLUSION: Combining pulsed RF with intradiscal ozone provides good clinical and radiological outcome in patients with cervical disc herniation and can be tried before open discectomy for patients with cervical disc herniation.

KEYWORDS: Cervical radiculopathy, Intradiscal ozone, Minimally invasive surgery, Pulsed Radiofrequency.

BACKGROUND

Cervical radiculopathy (CR) is a disabling medical condition characterized by radicular discomfort in one or both upper limbs, as well as sensory, motor, and reflex abnormalities in one or more of the affected nerve root distributions. Cervical radicular pain affects around 83 people out of every 100,000.[1] Retropulsed disc material, zygapophyseal joint enlargement, and other soft-tissue anomalies can all induce nerve root compression.[2]

Confirming the diagnosis of CR and ruling out myelopathy both require a comprehensive patient history and clinical examination.[3] Measures to treat cervical radiculopathy are either conservative or surgical.[4] Conservative measures to relieve the radicular neuropathic pain include pharmacological treatment and physiotherapy. Minimally invasive procedures include epidural or trans-foraminal injection of corticosteroids,[5] pulsed radiofrequency (PRF) of the dorsal root ganglion (DRG) and intradiscal ozone therapy. Options for surgical treatment include laminoforaminotomy, posterior laminectomy, and anterior cervical discectomy and fusion.

A decrease in the size of the herniated disc that is causing nerve root compression can be achieved through intradiscal ozone injection because it can hasten the breakdown of proteoglycans in the degenerated nucleus pulposus, leading to its reabsorption and dehydration.[6,7]

Previous research has been undertaken to assess the efficacy of PRF for treatment of radicular pain.[8] However, the size of disc herniation will not decrease using PRF resulting in continued mechanical compression of the nerve root as well as chemical irritation.

In this study, we theorized that adding intradiscal ozone therapy to PRF could improve the clinical outcome of the patients through inducing disc shrinkage resulting in relief of nerve root compression as well as decreasing chemical irritation.

The aim of this study was to compare between pulsed DRG RF at the cervical root combined with intradiscal ozone injection and PRF alone for treatment of patients with discogenic cervical radiculopathy.

PATIENTS AND METHODS

After approval of local Ethics Committee of Alexandria university (27/6/2020) and obtaining a written informed

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consent from each patient, the present study was carried out at Neurosurgery department, Alexandria University on 60 patients with cervical radiculopathy in a randomized controlled clinical trial.

We included patients with sustained discogenic radicular cervical pain failing to respond to best medical treatment for more than 4 weeks, pain severity more than 4 on numeric rating scale (NRS) with good response to cervical root block (50% pain reduction, measured on the NRS) and patients refusing surgery or unfit for surgery.

On the other hand we excluded patients with radicular motor weakness or cord compression manifestations, patients with previous cervical laminectomy or fusion, patients with deafferentation (neuropathic) pain caused by root injury (iatrogenic or pathological as diabetic neuropathy) and patients with uncontrolled coagulation disorders or active infection.

Patients meeting the described criteria were randomly allocated by a computer based program into three groups (20 patients each):

Group (I): Patients had PRF combined with intradiscal ozone

Group (II): Patients had PRF alone

Group (III): Control group which received only diagnostic blocks.

The procedure was performed in the operating room in supine position, using fluoroscopic guidance and strict aseptic technique. Vital measures such as pulse rate, electrocardiogram (ECG), noninvasive blood pressure, and oxygen saturation were measured throughout the procedure. 30 minutes before the surgery, 2 grams of ceftriaxone were given.

Technique for diagnostic cervical nerve root block

The diagnostic nerve block was performed with the patients lying supine and a fluoroscopy C-arm (Siemens, Germany) was used. The C-arm was positioned obliquely such that the X-rays were parallel to the axis of the intervertebral foramen. A 22-gauge cannula (10 or 15 cm SMK pole needle with 5 or 10 mm active curved tip) was introduced parallel to the beam of the X-rays. Following a change in the X-ray's direction to antero-posterior, the cannula was inserted further until its tip protruded just lateral to the facetal column. Following the use of contrast medium (omnipaque) to identify the segmental nerve, 0.5 mL of 2% xylocaine was gradually injected around the nerve. A diagnostic block was deemed successful if it reduced pain by at least 50% as measured by the NRS within Thirty minutes.

The levels that responded with the largest pain reduction were chosen for intervention (PRF combined with intradiscal ozone or PRF alone). Patients assigned to the control group underwent only diagnostic blocks

Technique for PRF of the cervical dorsal root ganglion

The same method as for the diagnostic blocks was employed. The approach was adjusted as needed while the cannula was still in the superficial subcutaneous layer, allowing it to lie over the dorsal part of the intervertebral foramen in the transition between the middle and most caudal third part. The cannula was inserted parallel to the X-ray beam. The vertebral artery, which is situated anterior to the ventral portion of the foramen, was taken into consideration when choosing this dorsal position. The X-rays were then switched to antero-posterior, and the cannula was inserted until its tip protruded over the facetal column.

The radiofrequency probe was then used in place of the stylet. The integrity of the RF system and proper electrode placement were confirmed by measuring the impedance between 250 and 500. Electrical stimulation at 50 Hz (sensory stimulation) was used to confirm the RF electrode. A tingling sensation in the corresponding dermatome had to be attained at less than 0.8V during stimulation. If the patient showed no sensory manifestations, the electrode was relocated. **(Fig. 1)**

The PRF current produced by the Cosman lesion generator (Cosman Medical, Inc., Burlington, MA, USA) was then passed through the electrode. The total duration of PRF was 120 seconds for 2 cycles.

Technique for intradiscal ozone injection

The patients were placed supine on the table with their arms at their sides and an anterolateral approach was used. The head and neck were slightly hyperextended to facilitate access to the cervical discs. It is important to stabilize the shoulders for better visibility of the lower cervical discs. The neurovascular bundle, particularly the carotid artery, and sternocleidomastoid muscle, were maneuvered laterally and manually protected, and the cannula entry point was positioned off the midline towards the patient's right side to make an anterolateral approach.

After the injection site was disinfected and local anesthesia was applied using xylocaine, a 22-gauge spinal needle was introduced by an anterolateral approach and gently pushed into the herniated vertebral disc under C arm control. Fluoroscopy imaging verified disc level in all cases. **(Fig. 1)**

A total of 2 to 4 mL of Oxygen-ozone mixture was injected with concentration of 30 µg/mL freshly prepared by Longevity Ozone Generator (Longevity Resources Inc., Sidney, British Columbia, Canada).[9] The ozone capacitance of the cervical disc is relatively small due to its smaller volume compared to the lumbar disc. Antibiotic injection was taken for ten days post intervention. Intradiscal ozone injection was combined with pulsed radiofrequency at the dorsal root ganglion in patients assigned in group I.

Patients were followed up for one year and were assessed immediately and at 1, 3, 6 and 12 months post intervention.

Follow up MRI cervical spine was done 3 months post intervention.

To verify the degree of change in pain reduction, the difference between the NRS pretreatment and 1, 3, 6 and 12 months after treatment was used to calculate the change in NRS. Based on the change in NRS, pain relief of at least 50% was considered successful.

The success or failure of the treatment 3 months after the intervention was the primary outcome measurement for our trial. Success was regarded as at least a 50% reduction in pain as measured by the NRS. A decrease in the NRS scale and the requirement for medication were used to measure improvement.

Secondary outcome measurements included all the primary outcome parameters but measured at 1 year after intervention. The influence of the treatment on the quality of life, was measured by the NDI (Neck Disability Index).[10] In order to find out if patients had undergone cervical spine surgery, they were contacted. Patients were also contacted to ask if they decreased the usage of pain medications or not.

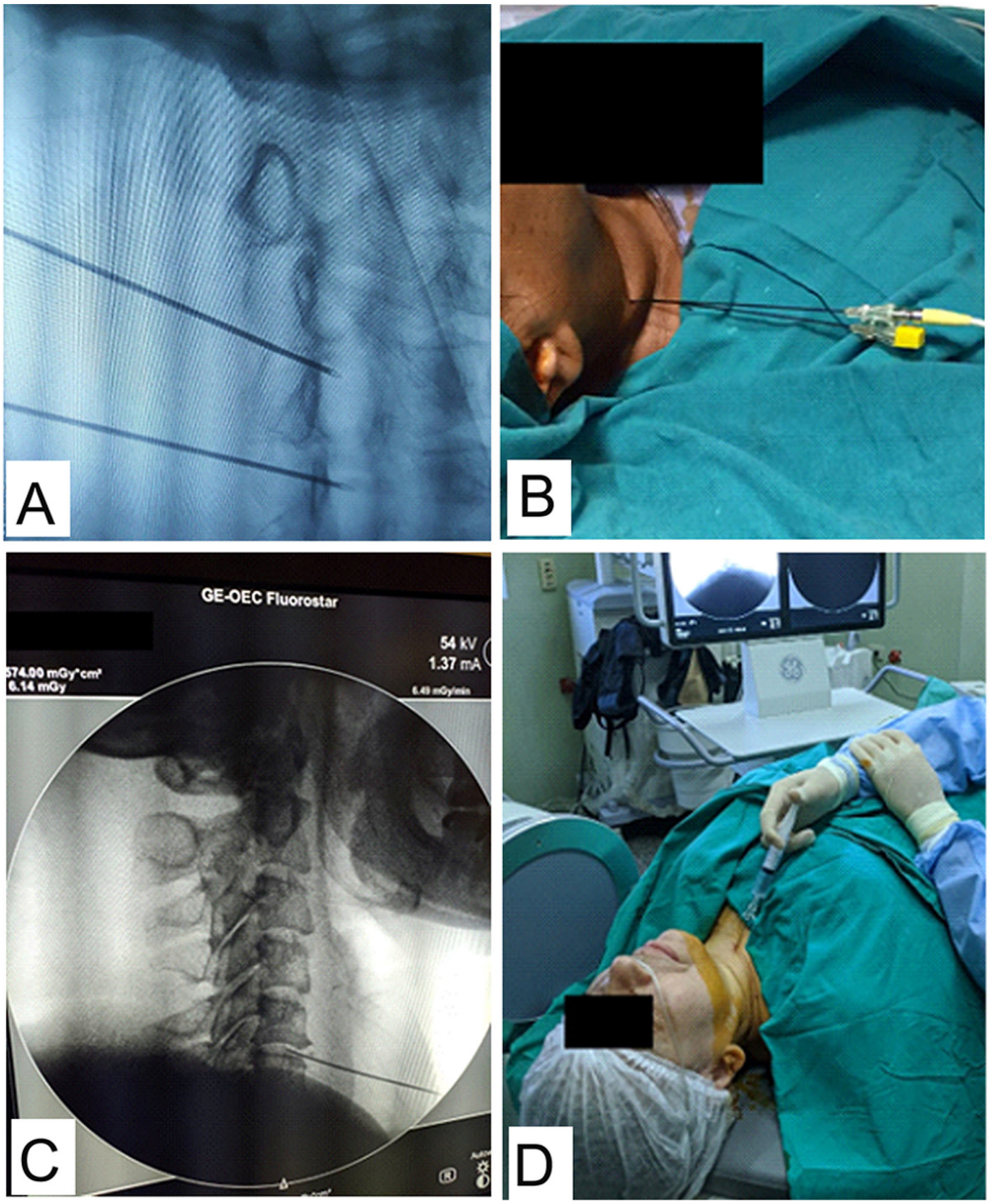

Fig 1: (A) X-ray image showing PRF at cervical DRG. (B) Position of patient and probe for dorsal root ganglion PRF. Also (C) X-Ray image showing spinal needle inserted in C5-6 cervical disc and (D) Position of patient and needle for intradiscal ozone.

Statistical analysis

With the aid of the statistical packages for social sciences (SPSS) version 20.0 (IBM Corp, Armonk, NY), data were fed into the computer and analysed. Categorical data were shown as percentages and numbers. Three groups were compared using a chi-square test. When more than 20% of the cells have an expected count of less than 5, the Monte Carlo correction test was instead used. The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to determine whether continuous data were normally distributed. For quantitative data that was normally distributed, the following expressions were used: range (minimum and maximum), mean, standard deviation, median, and interquartile range. The three study groups were compared using a one-way analysis of variance (ANOVA) test, which was then followed by a pairwise comparison using the Post Hoc test (Tukey), and a two-period comparison using the Paired t-test. While Friedman test was used to compare between more than two periods and Post Hoc Test (Dunn's) for pairwise comparisons for quantitative variables that were not normally distributed, Kruskal Wallis test was used to compare groups of non-normally distributed quantitative variables. The 5% level of significance was used to determine the results' significance.

Results

This prospective randomized controlled study was carried out on 60 patients with cervical radiculopathy admitted to Neurosurgery department, Alexandria University. Patients were randomized into three equal groups (20 patients each).

There were 12 (60%) females and 8 (40%) males in group I, 11 (55%) females and 9 (45%) males in group II and 13 (65%) females and 7 (35%) males in group III. There was no statistically significant difference between the three groups regarding sex (p= 0.812).

Twenty-five patients had duration of pain varying from 6 months to 1 year pre intervention (41.6%), 15 patients had duration of pain varying from 4 weeks to 6 months (25%), 13 patients had duration of pain varying from 1 to 2 years (21.6%) and 7 patients had duration of pain more than 2 years (11.6%).

There was no statistically significant difference in NRS between all three groups pre intervention. (p=0.741). Both groups I and II had statistically significant decrease in NRS when compared to group III where p values were 0.001 at 1 month, 3 months, 6 months and 1 year post intervention, with all NRS values shown in **(Table 1)**.

There was no statistically significant difference between group I and II according to NRS at 1 month (p=0.771), 3 months (p=0.667), 6 months (p=0.651) and 1 year (p=0.982) post intervention.

In group I, 15 (75%) patients had more than 50% reduction in NRS after 1 month, 16 (80%) patients after 3 months, 15 (75%) patients after 6 months and 14 (70%) patients after 1 year.

In group II, 14 (70%) patients had more than 50% reduction in NRS after 1 month, 14 (70%) patients after 3 months, 14 (70%) patients after 6 months and 13 (65%) patients after 1 year.

In group III, 7 (35%) patients had more than 50% reduction in NRS after 1 month, 6 (30%) patients after 3 months, 6 (30%) patients after 6 months and 5 (25%) patients after 1 year.

Both groups I and II had statistically significant difference in patients with more than 50% reduction in NRS when compared to group III, where p values were less than 0.001 at 1 month, 3 months, 6 months and 1 year post intervention.

There was no statistically significant difference between group I and II in patients with more than 50% reduction in NRS at 1 month (p=0.64), 3 months (p=0.717), 6 months (p=0.853) and 1 year (p=0.789) post intervention.

Both group I and II had statistically significant decrease in NDI at 1 year post intervention when compared to group III (p=0.001), however there was no statistically significant difference between group I and II as regard NDI at 1 year post intervention (p=0.964).

Only 1 patient (5 %) had cervical spine surgery in group I and II, while in group III, 5 patients (25%) had cervical spine surgery after 1 year of follow up, however the difference between three groups failed to reach statistical significance (p=0.192).

Fifteen patients (75%) in group I and 14 patients (70%) in group II reported decrease use of pain medications, while in group III 10 patients (50%) reported decrease use of pain medications, however the difference between three groups failed to reach statistical significance (p=0.215).

No serious complications were encountered in all 60 patients, only 5 patients (8.3%) had mild discomfort at the injection site 2 weeks after intervention which was relieved afterwards by analgesia. Those were two patients in group I, two patients in group II and one patient in group III.

We observed significant shrinkage of herniated disc fragment in MRI done 3 months after intervention in 5 patients in group I (PRF combined with intradiscal ozone) **(Figs. 2,3).** This reduction in disc size was observed in 5 patients (25%) in Group I, while in the other two groups, no appreciable changes were found.

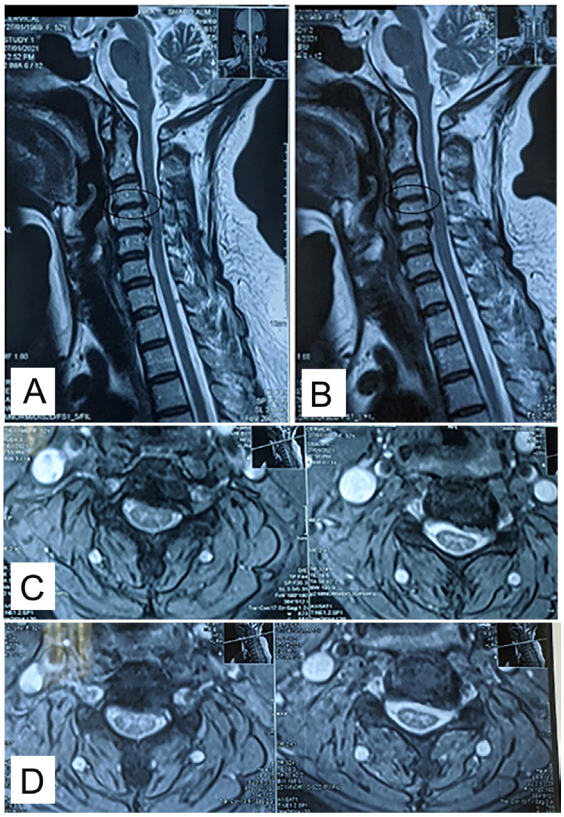

Fig 2: (A) Sagittal MRI cervical spine before the procedure and (B) MRI done 3 months after intradiscal ozone injection showing decrease in disc size (disc level 3-4), (C) MRI cervical spine axial view before the procedure and (D) MRI cervical spine axial view 3 months after intradisal ozone injection.

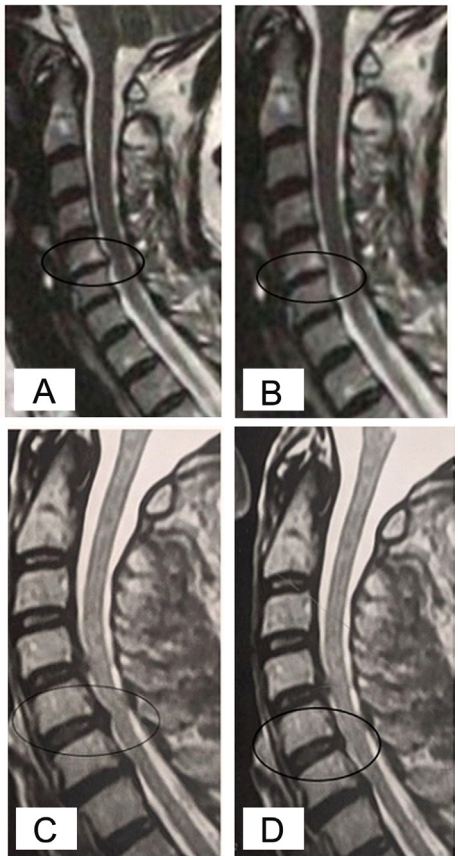

Fig 3: (A) Sagittal cervical MRI pre intervention and (B) 3 months post intradiscal ozone injection showing decrease in disc size (C5-6 disc). (C) Sagittal cervical MRI pre intervention and (D) 3 months post intradiscal ozone injection showing decrease in disc size (C5-6 disc).

Table 1: Comparison between the three studied groups according to VAS in each period

NRS	Group I (n = 20)	p_0	Group II (n = 20)	p_0	Group III (n = 20)	p_0	H	p
Pre-operative								
Min. – Max.	5 – 10		5 – 10		5 – 10			
Mean ± SD.	7.35 ± 1.60		7.15 ± 1.53		7 ± 1.52		0.599	0.741
Median (IQR)	7[a] (6 – 8)		7[a] (6 – 8)		7[a] (6 – 8)			
1 Month								
Min. – Max.	0 – 5		0 – 5		2 – 8			
Mean ± SD.	2.90 ± 1.29	<0.001*	3.10 ± 1.29	<0.001*	5 ± 1.86	<0.001*	14.622*	0.001*
Median (IQR)	3[b] (2.5 – 3.5)		3[b] (2 – 4)		5[a] (4 – 6)			
3 Months								
Min. – Max.	2 – 5		1 – 5		2 – 8			
Mean ± SD.	2.85 ± 0.88	<0.001*	2.95 ± 1.15	<0.001*	5.20 ± 24	<0.001*	17.862*	<0.001*
Median (IQR)	3[b] (2 – 3)		3[b] (2 – 4)		5[a] (4 – 7)			
6 Months								
Min. – Max.	2 – 6		1 – 5		2 – 8			
Mean ± SD.	3.20 ± 11	<0.001*	2.90 ± 1.17	<0.001*	5.35 ± 1.98	0.002*	18.446*	<0.001*
Median (IQR)	3[b] (3 – 3.5)		3[b] (2 – 4)		5[a] (4 – 7)			
1 Year								
Min. – Max.	2 – 6		1 – 6		2 – 9			
Mean ± SD.	3.40 ± 1.27	<0.001*	3.30 ± 1.17	<0.001*	5.60 ± 2.16	0.032*	14.911*	0.001*
Median (IQR)	3[b] (3 – 4)		3[b] (3 – 4)		6[a] (4 – 7.5)			

IQR: Inter quartile range. SD: Standard deviation. Min: Minimum. Max: Maximum.
H: H for Kruskal Wallis test, pairwise comparison between each 2 groups was done using Post Hoc Test (Dunn's for multiple comparisons test).
p: p value for comparing between the studied groups.
p0: p value for Post Hoc Test (Dunn's) for Friedman test for comparing between pre-operative and each other periods.
*: Statistically significant at $p \leq 0.05$.
Medians in the same row with any Common letter (a-b) are not significant (OR Medians with totally Different letters (a-b) are significant).
Group I: PRF combined with intradiscal ozone.
Group II: PRF alone.
Group III: Control.

DISCUSSION

We conducted this study on individuals with persistent cervical radicular pain since the existing data in the literature did not indicate the optimal treatment choice. Our study showed that PRF combined with intradiscal ozone and pulsed RF alone had good clinical outcome when compared to control group in terms of reduction of pain, need of medications, neck disability index and need for surgery, however the difference between both active treatments failed to reach statistical significance at 1 year follow up.

In our study, we compared two new active treatments (pulsed DRG RF at the cervical root combined with intradiscal ozone injection and pulsed RF alone) with a control group that received diagnostic blocks only. We chose to give the control group diagnostic blocks rather than just medical treatment in order to better evaluate the effectiveness of both active treatments offered, as patients tend to feel better if they receive diagnostic blocks. One reason for this is that positron emission tomography (PET) tests have shown that placebo and opioids stimulate the same brain area in the study carried out by Petrovic et al.[11]

In the control group, the mean NRS decreased from 7.0 to 5.0 after one month of treatment and 7 patients (35%) had more than 50% reduction in pain intensity after 1 month (which is considered a significant reduction). This period is too small to evaluate effectiveness of treatment and this improvement may be due to placebo effect or the natural course of the disease. This improvement was short lived and lost its significance later on where the mean increased to 5.2, 5.35, 5.6 at 3 months, 6 months

and 1 year respectively.

Successful treatment was defined as a reduction of pain by 50% or more when compared with NRS before intervention. In our study, 14 patients (70%) had a significant reduction in pain after one year of treatment when treated with intradiscal ozone combined with PRF, and 13 patients (65%) had a significant reduction in pain when treated with pulsed RF alone. The difference between those two groups failed to reach statistical significance, however both groups had a significant reduction in pain intensity and neck disability index when compared to the control group. No previous studies, to our knowledge, had combined intradiscal ozone therapy with PRF, which yielded good results in our study.

The results of our study as regards PRF are similar to previous studies as most of them showed clinically significant reduction in pain of 60% to 70% of patients.[12-14] The one-year follow-up period in our study provides confidence that the symptom reduction associated with both active treatments is not short term. In agreement with our study, one previous prospective study conducted by Choi et al.[15] showed that 66.7% of patients who were subjected to PRF had clinically significant pain reduction after 1 year follow up period.

Cervical spine MRI 3 months after ozone injection revealed a reduction in disc size in 5 cases (25%) in group I. Alexandre et al.[7] observed 39% reduction in herniated disc size 7 months after cervical intradiscal ozone. Also Zhang et al.[16] found highly significant correlation between lumbar herniated disc reduction, visual analogue scale, and patient satisfaction 6 months after lumbar intradiscal ozone injection.

The NDI decreased in group I from 20.8 to 12.1 (41.8%) and decreased in group II from 21.2 to 12.4 (41.5%). Both active treatments groups had significant reduction in NDI after 1 year and those results are better than those reported by Choi et al,[17] who stated that patients that were subjected to DRG PRF had 18.6% reduction in NDI after 3 months. It might be that we had better results because our follow up period for NDI was 1 year.

The overuse of strong analgesic drugs has repeatedly been recognized as a problem, resulting in increased morbidity and mortality in patients.[18] Ideally, interventional pain therapies would reduce or eliminate the requirement for prescription analgesics. In our study, 15 patients in group I (75%),14 patients in group II (70%) and 10 patients in group III (50%) who were taking medications prior to all procedures reduced or discontinued their use. Those results are comparable to the results reported by O'Gara et al,[14] who postulated that 69% of patients who had PRF at the cervical DRG decreased or discontinued pain medications.

Only 1 patient (5%) in group I and 1 patient (5%) in group II had cervical surgery while in group III 5 patients (25%) had cervical surgery. Although the difference between the three groups failed to reach statistical significance, pulsed RF and intradiscal ozone can decrease the need for conventional cervical surgeries. Those results are comparable to results found in the study conducted by O'Gara[14] who had 6% of patients having surgeries after failing to respond to PRF.

Combining intradiscal ozone injection with pulsed RF yielded mostly similar results as pulsed RF alone. This may give the impression that adding intradiscal ozone therapy to PRF has no added value and should be discarded. However, the insignificant difference between PRF with added intradiscal ozone and PRF alone that was observed at 1 year follow up is actually expected as PRF usually has significant results observed at this time frame of follow up. The added value of the intradiscal ozone therapy with the consequent reduction of the disc size could be obvious at a later time of follow up when the therapeutic effect of PRF wanes and the therapeutic response of disc size reduction by intradiscal ozone becomes more obvious.

CONCLUSION

A selective nerve root block with local anesthetic aids in the identification of the nerve root and dermatome affected but provides little therapeutic benefit.

Pulsed RF combined with intradiscal ozone and pulsed RF alone had good clinical outcome when compared to control group in terms of reduction of pain, need of medications, neck disability index and need for surgery, however the difference between both active treatments failed to reach statistical significance at 1 year follow up.

Combining pulsed RF with intradiscal ozone provides good clinical and radiological outcome in patients with cervical disc herniation and can be tried before open discectomy for those patients.

Further studies with larger cohort of patients and longer follow up period are needed to confirm or refute the validity of intradiscal ozone therapy as well as to compare it with other intradiscal cervical procedures.

List of abbreviations

ANOVA: Analysis of variance.
CR: Cervical radiculopathy.
CT: Computed Topography.
DRG: Dorsal root ganglion.
ECG: Electrocardiogram.
EMG: Electromyography.
MRI: Magnetic resonance imaging.
NDI: Neck disability index.
NRS: Numeric rating scale.
PET: Positron emission tomography.
PRF: Pulsed radiofrequency.
RF: Radiofrequency.
SPSS: Statistical packages for social sciences.

Disclosure

The authors report no conflict of interest in the materials

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